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Plant Coumarins: VI.* Synthesis of 3-Vinylfurocoumarin Derivatives Based on Oreoselone

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Abstract—Palladium-catalyzed Heck reaction of oreoselone trifluoromethanesulfonate with various terminal alkenes (methyl acrylate, styrene, vinylpyridines, *N*-vinylpyrrole, and *N*-vinyl-1,2,4-triazole) led to the formation of the corresponding (*E*)-3-vinyl-7*H*-furo[3,2-*g*]chromen-7-ones. The yield was found to depend on the catalytic system and initial olefin structure.

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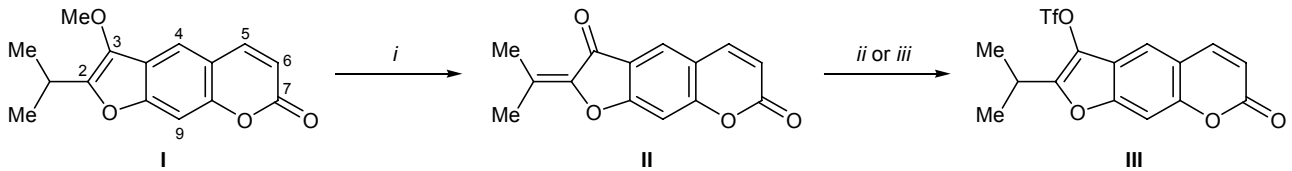
Interest in linearly fused furocoumarins is determined by important role of these compounds in vital activity of plants and animals, as well as by their strong and diverse biological activity. Such furocoumarins as psoralens exert various biological effects on eukaryotic cells (inhibit cell division in the G-2 and S-phases and induce apoptosis) and are used in therapy of skin diseases (PUVA therapy) [2, 3]. Studies on structure–activity relationships showed that introduction of additional substituents into the 3-position of the furocoumarin system reduces phototoxic effect (skin phototoxicity) of fused psoralens [3]. 3-Aryl-substituted furocoumarins were found to possess cardiotropic activity [4]. A number of metabolites of the dihydrofurocoumarin series containing a substituent on C^3 were isolated and found to exhibit vasodilator activity [5].

The goal of the present work was to synthesize new furocoumarin derivatives having various substituents on C^3 from an accessible plant coumarin, peucedanin (**I**) [6]. Treatment of peucedanin (**I**) with hydrochloric acid in methanol quantitatively afforded oreoselone (**II**) which reacted with trifluoromethanesulfonic anhydride in the presence of a base to give 2-isopropyl-7-oxo-7*H*-furo[3,2-*g*]chromen-3-yl trifluoromethanesulfonate (**III**) in up to 72% yield (Scheme 1). The structure of oreoselone trifluoromethanesulfonate **III** was proved by X-ray analysis.

Furocoumarins having functionalized olefinic fragments in the furan ring were synthesized by the Heck reaction [7] of trifluoromethanesulfonate **III** with various terminal alkenes. Initially, the reaction of **III** with methyl acrylate (**IV**) was carried out using $Pd(OAc)_2$/(*o*-Tol)$_3$P (2/8 mol %) as catalytic system, which was shown to be effective in the cross coupling of functionally substituted bromides with acrylates; triethylamine was used as base, and dimethylformamide, as solvent [8]; however, 3-(3-methoxy-3-oxoprop-1-en-1-yl) derivative **V** was obtained in a poor yield. It was more effective to use as ligand tris(*tert*-butyl)phos-

Scheme 1.

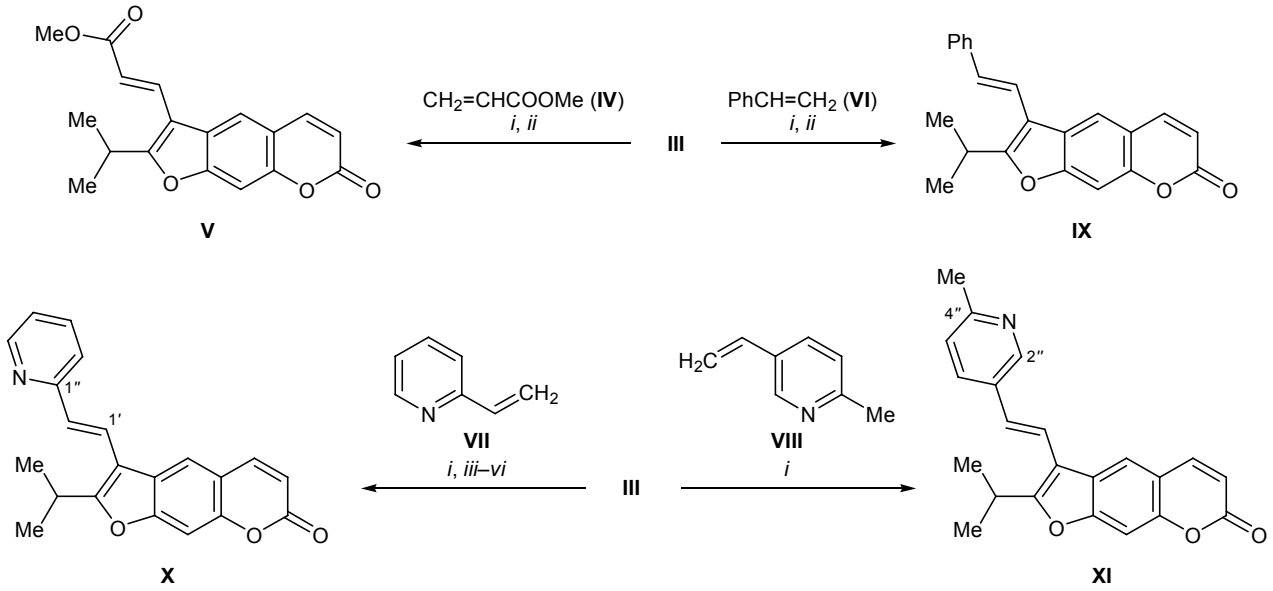


I II III

i: Concentrated hydrochloric acid, MeOH, 55°C; *ii*: $(CF_3SO_2)_2O$, pyridine, –10°C (30 min), 25°C (12 h); *iii*: $(CF_3SO_2)_2O$, 2,4,6-trimethylpyridine, CH_2Cl_2, 10°C (10 min), 25°C (16 h).

* For communication V, see [1].

Scheme 2.



i: $Pd(OAc)_2$, (*o*-Tol)$_3$P, Et_3N, DMF, 115°C; *ii*: $Pd(OAc)_2$, (*t*-Bu)$_3$P, Et_3N, DMF, 115°C; *iii*: $Pd(OAc)_2$, BINAP, Et_3N, DMF, 115°C; *iv*: $Pd(dba)_2$, (*o*-Tol)$_3$P, Et_3N, DMF, 115°C; *v*: $Pd(dba)_2$, BINAP, Et_3N, DMF, 115°C; *vi*: $Pd(dba)_2$, BINAP, *t*-BuONa, dioxane, 100°C.

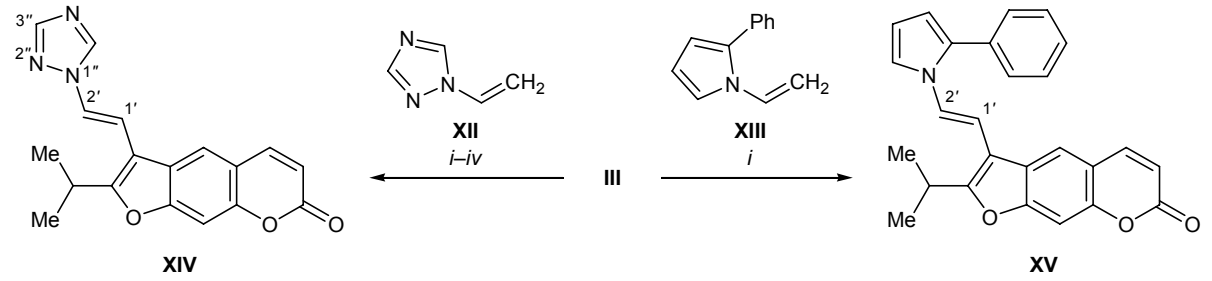
phine; in this case, the yield of **V** was 42%, and the optimal ratio $Pd(OAc)_2$/(*t*-Bu)$_3$P was 2/8 mol % (Scheme 2). It should be noted that in all cases the conversion of the initial compound was complete.

By condensation of furocoumarin trifluoromethanesulfonate **III** with styrene **VI** or vinylhetarenes [2-vinylpyridine (**VII**) and 2-methyl-5-vinylpyridine (**VIII**)] in DMF on heating to 115°C in the presence of $Pd(OAc)_2$/(*o*-Tol)$_3$P (2/8 mol %) as catalytic system we obtained (*E*)-2-isopropyl-3-styryl- and (*E*)-2-isopropyl-3-[pyridinyl)vinyl]-7*H*-furo[3,2-*g*]chromen-7-ones **IX**–**XI** (Scheme 2; yield 38–45%). Interestingly, the reaction of **III** with styrene **VI** at 80°C gave no more than 10% of condensation product **IX**. Replacement of the ligand by tris(*tert*-butyl)phosphine (*ii*) in the reaction of **III** with styrene (**VI**) or by BINAP (*iii*) in the reaction with 2-vinylpyridine (**VII**) did not improve the yield of condensation products **IX** and **X**. Bis(dibenzylideneacetone)palladium [$Pd(dba)_2$] (5 mol %) in combination with (*o*-Tol)$_3$P or BINAP (10 mol %) as ligand ensured, respectively, only 28 or 23% yield of **X**. By reaction of compound **III** with 2-vinylpyridine (**VII**) in dioxane in the presence of $Pd(dba)_2$/BINAP (5/10 mol %) and sodium *tert*-butoxide we obtained 20% of 3-[2-(pyridin-2-yl)vinyl]furocoumarin **X**. Thus the best yields in the Heck reactions of trifluoromethanesulfonate **III** with vinylarenes **VI**–**VIII** were attained using $Pd(OAc)_2$/(*o*-Tol)$_3$P as catalytic system.

Taking into account interest in psoralen derivatives having an aza heteroring fused to the furan ring [9], we examined cross coupling of trifluoromethanesulfonate **III** with *N*-vinyl-substituted heterocyclic compounds, 1-vinyl-1*H*-1,2,4-triazole (**XII**) and 2-phenyl-1-vinyl-1*H*-pyrrole (**XIII**) (Scheme 3). The condensation of **III** with vinyltriazole **XII** in the presence of $Pd(OAc)_2$/(*o*-Tol)$_3$P (2/8 mol %) gave (*E*)-3-[2-(1*H*-1,2,4-triazol-1-yl)vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (**XIV**) in 48% yield; according to the ^{1}H NMR data, the reaction mixture also contained a small amount (no more than 3%) of the corresponding *Z* isomer. In the reaction of **III** with pyrrole **XIII** under analogous conditions we isolated 42% of (*E*)-3-[2-(2-phenyl-1*H*-pyrrol-1-yl)-vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (**XV**), and only traces of its *Z* isomer were detected. Replacement of the ligand in the catalytic system by BINAP or (*t*-Bu)$_3$P in the condensation of **III** with **XII** did not increase the fraction of the *Z* isomer, but the yield of the *E* isomer was considerably lower. An efficient catalyst for the condensation of compound **III** with vinyltriazole **XII** was dichlorobis(triphenylphosphine)-palladium (5 mol %); the yield of (*E*)-3-[2-(1*H*-1,2,4-triazol-1-yl)vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (**XIV**) was 40%.

The structure of the synthesized compounds was determined on the basis of their spectral parameters and elemental composition. The structure of oreo-

Scheme 3.



i: $Pd(OAc)_2$, (*o*-Tol)$_3$P, Et_3N, DMF, 115°C; *ii*: $Pd(OAc)_2$, BINAP, Et_3N, DMF, 115°C; *iii*: $Pd(OAc)_2$, (*t*-Bu)$_3$P, Et_3N, DMF, 115°C; *iv*: $Pd(PPh_3)_2Cl_2$, Et_3N, DMF, 125°C.

selone trifluoromethanesulfonate **III** was proved by X-ray analysis. A unit cell of compound **III** in crystal contains two independent molecules, one of which is shown in figure. The bond lengths and bond angles in the two independent molecules coincide within 3σ and approach the corresponding standard values [10]. The tricyclic skeleton in both molecules is almost planar. The mean-square deviation from the plane is 0.029 Å for one molecule, and 0.046 Å, for the other.

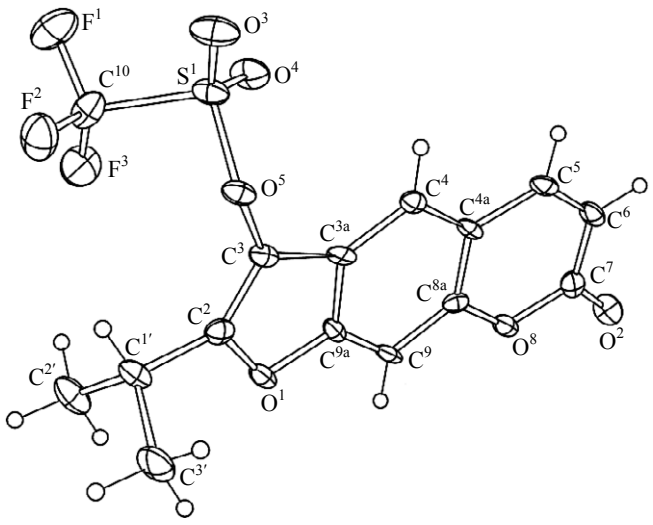
Molecules **III** in crystal are linked to couples via π-stacking interaction [intercentroid distance 3.665(3) Å, interplanar distance 3.27 Å], and these couples are packed to form parquet-like pattern through C^{9a}–$H^{9aa}\cdots O^{2b}$ hydrogen bonds [$H^{9aa}\cdots O^{2b}$ 2.37, $C^{9a}\cdots O^{2b}$ 3.262(7) Å, $\angle C^{9a}H^{9aa}O^{2b}$ 155°]. In addition, molecules **III** are linked to each other via numerous $O\cdots\pi$ interactions [the distance between the oxygen atom and the centroid of the neighboring π-system ranges from 3.150(4) to 3.504(5) Å].

Oreoselone trifluoromethanesulfonate **III** and Heck coupling products **V**, **IX**–**XI**, **XIV**, and **XV** are characterized by electronic absorption spectra typical of coumarin derivatives. For example, the spectrum of **III** contains absorption bands with their maxima at λ 250, 284, and 337 nm. The cross-coupling products displayed in the UV spectra a larger number of absorption bands and increased intensity of absorption maxima due to extension of conjugation chain. For instance, the spectrum of **IX** contains absorption maxima at λ 222, 232, 255, 301, 310, 344, and 352 nm. The ^{1}H and ^{13}C NMR spectra of the synthesized compounds were consistent with the assumed structures; only one set of signals from the furocoumarin skeleton and the corresponding substituent was observed. Protons at the exocyclic double C=C bond (1′-H and 2′-H) resonated in the ^{1}H NMR spectra of condensation products **V**, **IX**–**XI**, **XIV**, and **XV** as doublets at δ 6.88–7.04 and 7.11–7.66 or 6.64–7.16 and 6.98–7.44 ppm. The coupling constant for 1′-H and 2′-H in compounds **V** and **IX**–**XI** (J = 15.1–16.2 Hz) and hetarylvinyl derivatives **XIV** and **XV** (J = 12.8–14.2 Hz) indicates *trans* configuration of the exocyclic double bond.

Thus Heck reaction of oreoselone trifluoromethanesulfonate with various alkenes may be used to synthesize various 3-substituted derivatives of a linearly fused furocoumarin, peucedanin; the products attract interest as potential biologically active substances.

EXPERIMENTAL

The NMR spectra were recorded from solutions in $CDCl_3$ or $CDCl_3$–CD_3OD on Bruker AV-300 [300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C), AV-400 [400.13 MHz for ^{1}H and 100.78 MHz for ^{13}C), and AV-600 spectrometers (600.30 MHz for ^{1}H and 150.96 MHz for ^{13}C). Signals in the NMR spectra were assigned using various proton–proton and carbon–



Structure of 2-isopropyl-7-oxo-7*H*-furo[3,2-*g*]chromen-3-yl trifluoromethanesulfonate (**III**) according to the X-ray diffraction data.

proton shift correlation techniques (COSY, XHCO, COLOC). Signal multiplicities in the ^{13}C NMR spectra were determined using *J* modulation technique. The IR spectra were recorded in KBr on a Bruker Vector-22 spectrometer. The UV spectra were measured on an HP 8453 UV-Vis spectrophotometer. The elemental compositions were determined on a Carlo Erba 1106 CHN-analyzer.

The X-ray diffraction data for compound **III** were acquired at –100°C on a Bruker Kappa Apex II diffractometer with a two-coordinate CCD detector (MoK_α irradiation, graphite monochromator, ω–φ scanning up to 2θ = 51°). Analysis of the geometric parameters and intermolecular interactions was performed using PLATON [11] and MERCURY programs [12].

The products were isolated by column chromatography on silica gel (0.035–0.070 mm, Acros Organics) or aluminum oxide using chloroform or chloroform–ethanol (50:3) as eluent. The progress of reactions was monitored by TLC on Silufol UV-254 plates using chloroform–ethanol (3:1) or benzene as eluent; spots were visualized by treatment with iodine vapor and under UV light.

Commercial (*o*-Tol)$_3$P, (*R*)-(+)BINAP, (*t*-Bu)$_3$P, and trifluoromethanesulfonic anhydride (Alfa Aesar) were used. The solvents (dioxane, DMF, and CH_2Cl_2), Et_3N, 2-methyl-5-vinylpyridine, 2-vinylpyridine, styrene, and methyl acrylate were distilled in a stream of argon just before use; $Pd(OAc)_2$ was synthesized as described in [13]; $Pd(dba)_2$ was prepared according to the procedure reported in [14] and was used without recrystallization; $Pd(PPh_3)_2Cl_2$ was synthesized as reported in [15]; oreoselone was prepared by hydrolysis of peucedanin [16]; peucedanin was isolated from *Peucedanum morisonii* roots according to [6].

2-Isopropyl-7-oxo-7*H*-furo[3,2-*g*]chromen-3-yl trifluoromethanesulfonate (III). *a*. A solution of 500 mg (2 mmol) of oreoselone (**II**) in 3 ml of anhydrous pyridine was cooled to (–10°C), 2.256 g (8 mmol) of trifluoromethanesulfonic anhydride was added dropwise under argon, and the mixture was stirred for 30 min at –10°C, allowed to warm up to room temperature, and stirred for 12 h under argon. When the reaction was complete (TLC), the mixture was treated with 5 ml of water and extracted with diethyl ether (5×10 ml). The extracts were combined, washed with water (2×10 ml), dried over $MgSO_4$, and evaporated, and the residue was additionally dried by azeotropic distillation with benzene and recrystallized from diethyl ether. Yield 0.54 g (72%).

b. Oreoselone (**II**), 500 mg (2 mmol), was dissolved in 10 ml of anhydrous methylene chloride, 290 mg (2.4 mmol) of 2,4,6-trimethylpyridine was added under argon, the mixture was cooled to 10°C, 1.128 g (4 mmol) of trifluoromethanesulfonic anhydride was added dropwise at 10–20°C, and the mixture was stirred for 16 h. The mixture was then treated with 8 ml of water, the organic phase was separated, and the aqueous phase was extracted with methylene chloride (4×5 ml). The extracts were combined with the organic phase, washed with water, dried over $MgSO_4$, and evaporated to isolate 0.52 g (69%) of compound **III** with mp 132–133°C (from diethyl ether). IR spectrum, ν, cm^{-1}: 3487, 2929, 2857, 1665, 1640, 1626, 1600, 1280, 1253, 1174, 1110, 1050, 1037, 767, 645. UV spectrum ($CHCl_3$), λ_{max}, nm (log ε): 250 (4.29), 284 (3.80), 337 (3.73). ^1H NMR spectrum, δ, ppm: 1.04 d [6H, (C**H**$_3$)$_2$CH, *J* = 7 Hz], 2.93 m [1H, C**H**(CH$_3$)$_2$], 6.08 d (1H, 6-H, *J* = 9.8 Hz), 6.95 s (1H, 9-H), 7.07 s (1H, 4-H), 7.50 d (1H, 5-H, *J* = 9.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.95 q [(**C**H$_3$)$_2$CH], 23.48 d [**C**H(CH$_3$)$_2$], 101.12 d (C^9), 114.05 d (C^6), 114.19 s (C^{4a}), 121.52 d (C^4), 125.99, 127.70, 129.41, 131.12 q (CF_3), 125.62 s (C^3), 143.51 s (C^{3a}), 144.39 d (C^5), 151.18 s (C^{8a}); 160.04 s, 160.49 s, and 161.74 s (C^2, C^7, C^{9a}). ^{19}F NMR spectrum (relative to C_6F_6 as internal reference): δ_F 89.12 ppm, s (CF_3). Found, %: C 47.03; H 2.99; F 15.08; S 8.30. $C_{15}H_{11}F_3O_6S$. Calculated, %: C 47.88; H 2.95; F 15.15; S 8.52.

Methyl (*E*)-3-(2-isopropyl-7-oxo-7*H*-furo[3,2-*g*]-chromen-3-yl)prop-2-enoate (V). *a*. Oreoselone trifluoromethanesulfonate **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 118 mg (1.3 mmol) of methyl acrylate, 2.2 mg (2 mol %) of $Pd(OAc)_2$, 30 mg (8 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 5 h at 115°C (until initial compound **III** disappeared according to the TLC data). The mixture was cooled under argon and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent. The amount of the product thus isolated was insufficient for further purification.

b. Oreoselone trifluoromethanesulfonate **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 118 mg (1.3 mmol) of methyl acrylate, 2.2 mg (2 mol %) of $Pd(OAc)_2$, 10 mg (8 mol %) of (*t*-Bu)$_3$P, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 7 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column

chromatography on silica gel using chloroform as eluent. Recrystallization from chloroform gave 88 mg (42%) of compound **V**. No *Z* isomer was detected by ^{1}H NMR spectroscopy. mp 113–114°C. IR spectrum, ν, cm^{-1}: 1741, 1625, 1590, 1391, 1369, 1195, 1139, 1100, 1020, 938, 816, 742, 638. UV spectrum ($CHCl_3$), λ_{max}, nm (log ε): 253 (3.90), 295 (3.49), 309 (3.47), 340 (3.48), 354 (3.45). ^{1}H NMR spectrum, δ, ppm: 0.92 d and 1.02 d [3H each, (C**H**$_3$)$_2$CH, *J* = 7.0 Hz], 2.58 m [1H, C**H**(CH$_3$)$_2$], 3.56 s (3H, OCH$_3$) 6.23 d (1H, 6-H, *J* = 9.6 Hz), 6.74 s (1H, 9-H), 6.84 d (1H, 2′-H, *J* = 15.5 Hz), 7.53 d (1H, 5-H, *J* = 9.6 Hz), 7.66 d (1H, 1′-H, *J* = 15.5 Hz), 7.88 s (1H, 4-H). ^{13}C NMR spectrum, δ_C, ppm: 20.65 q [(**C**H$_3$)$_2$CH], 26.96 d [**C**H(CH$_3$)$_2$], 51.39 q (OCH$_3$), 99.54 d (C^9), 111.85 s and 112.33 s (C^3, C^{4a}), 115.63 d and 116.18 d (C^4, C^6), 121.28 s (C^{3a}), 128.53 d (C$^{2'}$), 143.54 d and 144.40 d (C^5, C$^{1'}$), 150.40 s and 151.22 s (C^{8a}, C^{9a}), 158.05 s (C^2), 159.49 s (C^7), 167.17 s (C$^{3'}$). Found, %: C 68.85; H 5.25. $C_{18}H_{16}O_5$. Calculated, %: C 69.22; H 5.16.

2-Isopropyl-3-[(*E*)-2-phenylvinyl]-7*H*-furo-[3,2-*g*]chromen-7-one (IX). *a*. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 135 mg (1.3 mmol) of styrene (**VI**), 2.2 mg (2 mol %) of Pd(OAc)$_2$, 32 mg (8 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et$_3$N were added under argon, and the mixture was heated for 7 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent. Recrystallization from diethyl ether gave 80 mg (40%) of **IX**. When the reaction was carried out at 80°C (7 h), evaporation of the solvent and subsequent chromatographic separation (silica gel, chloroform) gave a fraction containing 88% of initial compound **III** and a fraction containing 10% of compound **IX**.

b. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 135 mg (1.3 mmol) of styrene (**VI**), 2.2 mg (2 mol %) of Pd(OAc)$_2$, 10 mg (8 mol %) of (*t*-Bu)$_3$P, and 0.07 ml (1.3 equiv) of Et$_3$N were added under argon, and the mixture was heated for 7 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent. Yield 72 mg (33%), mp 133–134°C. IR spectrum, ν, cm^{-1}: 3082, 3060, 3026, 1730, 1678, 1625, 1577, 1491, 1353, 1286, 1216, 1140, 1100, 1046, 1031, 950, 907, 850, 825, 807, 756, 700, 666. UV spectrum ($CHCl_3$), λ_{max}, nm (log ε): 243 (3.41), 249 (3.40), 253 (3.39), 264 sh (3.23), 330 sh (2.97), 355 (2.62). ^{1}H NMR spectrum, δ, ppm: 1.43 d [6H, (C**H**$_3$)$_2$CH, *J* = 7.0 Hz], 3.15 m [1H, C**H**(CH$_3$)$_2$], 6.27 d (1H, 6-H, *J* = 9.7 Hz), 6.99 s (1H, 9-H), 7.06 d (1H, 2′-H, *J* = 15.0 Hz), 7.14 d (1H, 1′-H, *J* = 15.0 Hz), 7.29 m (1H, 4″-H), 7.34 m (2H, 3″-H, 5″-H), 7.37 s (1H, 4-H), 7.61 d (2H, 2″-H, 6″-H), 7.71 d (1H, 5-H, *J* = 9.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 18.41 q [(**C**H$_3$)$_2$CH], 27.09 d [C**H**(CH$_3$)$_2$], 99.99 d (C^9), 114.11 d (C^6), 114.33 s (C^{4a}), 117.05 s (C^{3a}), 120.58 d (C^4), 126.90 d (C$^{1'}$), 127.47 d (C$^{2''}$ C$^{6''}$), 128.06 d (C$^{3''}$, C$^{5''}$), 128.69 s (C^3), 128.99 d (C$^{4''}$) 132.90 d (C$^{2'}$), 136.82 s (C$^{1''}$), 144.48 d (C^5), 144.54 s (C^{8a}), 151.31 s (C^{9a}), 159.32 s (C^2), 160.36 s (C^7). Found, %: C 79.45; H 5.25. $C_{22}H_{18}O_3$. Calculated, %: C 79.98; H 5.49.

2-Isopropyl-3-[(*E*)-2-(pyridin-2-yl)vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (X). *a*. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 136 mg (1.3 mmol) of 2-vinylpyridine (**VII**), 2.2 mg (2 mol %) of Pd(OAc)$_2$, 32 mg (8 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et$_3$N were added under argon, and the mixture was heated for 8 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent. The subsequent recrystallization from diethyl ether gave 100 mg (38%) of compound **X**.

b. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 136 mg (1.3 mmol) of 2-vinylpyridine (**VII**), 2.2 mg (2 mol %) of Pd(OAc)$_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et$_3$N were added under argon, and the mixture was heated for 7 h at 115°C (TLC) and treated as described above to isolate 93 mg (35%) of compound **X**.

c. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 211 mg (2 mmol) of 2-vinylpyridine (**VII**), 21 mg (5 mol %) of Pd(dba)$_2$, 46 mg (10 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et$_3$N were added under argon, and the mixture was heated for 7 h at 115°C and treated as described above to isolate 50 mg (18%) of compound **X**.

d. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 211 mg (2 mmol) of 2-vinylpyridine (**VII**), 21 mg (5 mol %) of Pd(dba)$_2$, 42 mg (10 mol%) of BINAP, and 0.07 ml (1.3 equiv) of Et$_3$N were added under argon, and the mixture was heated for 7 h at 115°C and treated as described above to isolate 62 mg (23%) of compound **X**.

e. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous dioxane, 211 mg (2 mmol) of 2-vinylpyridine (**VII**), 21 mg (5 mol %) of Pd(dba)$_2$,

42 mg (10 mol %) of BINAP, and 84 mg (1.3 equiv) of *t*-BuONa were added under argon, and the mixture was heated for 9 h at 105°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent. Recrystallization from diethyl ether gave 44 mg (15%) of compound **X**, mp 201–202°C. IR spectrum, ν, cm^{-1}: 1732, 1715, 1626, 1571, 1353, 1289, 1148, 1097, 1066, 919, 881, 826, 756, 742, 689, 668, 654. UV spectrum ($CHCl_3$), λ_{max}, nm (logε): 255 (4.60), 301 (4.20), 310 (4.20), 344 (4.23). ^{1}H NMR spectrum, δ, ppm: 1.42 d [6H, (CH_3)$_2$CH, *J* = 7.0 Hz], 3.15 m [1H, C**H**(CH_3)$_2$], 6.26 d (1H, 6-H, *J* = 9.7 Hz), 6.98 s (1H, 9-H), 7.06 d (1H, 2′-H, *J* = 16.1 Hz), 7.18 m (1H, 4″-H), 7.37 s (1H, 4-H), 7.49 d (1H, 6″-H, *J* = 8.0 Hz), 7.70 d (1H, 5-H, *J* = 9.7 Hz), 7.73 d.d (1H, 5″-H, *J* = 7.8, 8.0 Hz), 7.82 d (1H, 1′-H, *J* = 16.1 Hz), 8.52 d (1H, 3″-H, *J* = 7.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.73 q [(CH_3)$_2$CH], 27.04 d [CH(CH_3)$_2$], 99.11 d (C^9), 114.06 s (C^{4a}), 114.39 d (C^6), 115.48 s (C^{3a}), 120.53 d (C^4), 120.88 d and 121.60 d ($C^{2''}$, $C^{6''}$), 128.94 d ($C^{1'}$), 130.77 s (C^3), 131.88 d ($C^{2'}$), 136.33 d ($C^{5''}$), 144.48 d (C^5), 149.22 d ($C^{3''}$), 149.34 s (C^{8a}), 151.20 s (C^{9a}), 154.95 s ($C^{1''}$), 159.14 s (C^2), 160.52 s (C^7). Found, %: C 57.79; H 4.21; Cl 23.12; N 3.12. $C_{21}H_{17}NO_3 \cdot CHCl_3$. Calculated, %: C 58.21; H 3.97; Cl 23.60; N 3.09.

2-Isopropyl-3-[(*E*)-2-(4-methylpyridin-3-yl)-vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (XI). Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 153 mg (1.3 mmol) of 2-methyl-5-vinylpyridine (**VIII**), 2.2 mg (2 mol %) of $Pd(OAc)_2$, 32 mg (8 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 8 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected by column chromatography on aluminum oxide using chloroform–ethanol (50:3), and the isolated fraction was subjected to repeated chromatography on silica gel using chloroform as eluent. Yield 87 mg (38%), oily substance. IR spectrum, ν, cm^{-1}: 1733, 1710, 1648, 1620, 1574, 1541, 1491, 1291, 1260, 1203, 1143, 1098, 1036, 826, 689, 669, 651. UV spectrum ($CHCl_3$), λ_{max}, nm (logε): 244 (4.14), 275 sh (3.99), 300 (3.54), 331 (3.96). ^{1}H NMR spectrum, δ, ppm: 1.42 d [6H, (CH_3)$_2$CH, *J* = 7.0 Hz], 3.19 m [1H, C**H**(CH_3)$_2$], 2.54 s (3H, CH_3), 6.30 d (1H, 6-H, *J* = 9.7 Hz), 6.98 d (1H, 2′-H, *J* = 16.2 Hz), 7.02 s (1H, 9-H), 7.16 d (1H, 1′-H, *J* = 16.2 Hz), 7.31 d (1H, 5″-H, *J* = 8.0 Hz), 7.41 s (1H, 4-H), 7.54 d (1H, 5-H, *J* = 9.7 Hz), 8.02 d.d (1H, 6″-H, *J* = 8.0, 2.0 Hz), 8.96 d (1H, 2″-H, *J* = 2.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 20.71 q [(CH_3)$_2$CH], 23.36 q (4″-CH_3), 27.02 d [CH(CH_3)$_2$], 99.48 d (C^9), 114.04 s (C^{4a}), 114.27 d (C^6), 117.42 s (C^{3a}), 120.51 d (C^4), 122.13 d ($C^{5''}$), 127.82 s ($C^{1''}$), 129.38 d ($C^{1'}$), 130.55 s (C^3), 132.21 d ($C^{2'}$), 133.43 d ($C^{6''}$), 144.47 d (C^5), 146.22 d ($C^{2''}$), 151.18 s (C^{8a}), 151.28 s (C^{9a}), 157.84 s ($C^{4''}$), 159.12 s (C^2), 160.86 s (C^7). Found, %: C 72.71; H 5.82; N 3.68. $C_{22}H_{19}NO_3 \cdot H_2O$. Calculated, %: C 72.73; H 5.78; N 3.85.

2-Isopropyl-3-[(*E*)-2-(1*H*-1,2,4-triazol-1-yl)-vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (XIV). *a*. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 123 mg (1.3 mmol) of 1-vinyl-1*H*-1,2,4-triazole (**XII**), 2.2 mg (2 mol %) of $Pd(OAc)_2$, 32 mg (8 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 8 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent to isolate a fraction containing compound **XIV** and a small amount of its *Z* isomer (according to the ^{1}H NMR data). Recrystallization from diethyl ether gave 100 mg (48%) of **XIV**.

b. Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 123 mg (1.3 mmol) of 1-vinyl-1*H*-1,2,4-triazole (**XII**), 4.4 mg (4 mol %) of $Pd(OAc)_2$, 34 mg (8 mol %) of BINAP, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 8 h at 115°C (TLC) and treated as described above in *a* to isolate 96 mg (45%) of compound **XIV**.

c. Compound **III**, 250 mg (0.67 mmol), was dissolved in 3 ml of anhydrous DMF, 123.5 mg (1.3 mmol) of 1-vinyl-1*H*-1,2,4-triazole (**XII**), 23 mg (5 mol %) of $Pd(PPh_3)_2Cl_2$, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 5 h at 115°C (TLC) and treated as described above in *a* to isolate 86 mg (40%) of compound **XIV**.

d. Compound **III**, 250 mg (0.67 mmol), was dissolved in 3 ml of anhydrous DMF, 123 mg (1.3 mmol) of 1-vinyl-1*H*-1,2,4-triazole (**XII**), 2.2 mg (2 mol %) of $Pd(OAc)_2$, 10 mg (8 mol %) of tris(*tert*-butyl)-phosphine, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 5 h at 115°C (TLC) and treated as described above in *a* to isolate 42 mg (20%) of compound **XIV**, mp 181–184°C. IR spectrum, ν, cm^{-1}: 3432, 3124, 3059, 2853, 1726, 1628, 1577, 1142, 1190, 1219, 1274, 1510, 1458, 1392, 1347, 1318, 1070, 1043, 1002, 960, 935,

900, 876, 827, 778, 671. UV spectrum ($CHCl_3$), λ_{max}, nm (log ε): 259 (4.27), 302 (4.23), 348 sh (3.73). ^{1}H NMR spectrum, δ, ppm: 1.21 d [6H, (C**H**$_3$)$_2$CH, *J* = 7.0 Hz], 3.19 [1H, C**H**(CH$_3$)$_2$], 6.21 d (1H, 6-H, *J* = 9.7 Hz), 7.06 s (1H, 9-H), 7.16 d (1H, 2′-H, *J* = 14.2 Hz), 7.41 d (1H, 1′-H, *J* = 14.2 Hz), 7.57 s (1H, 4-H), 7.65 d (1H, 5-H, *J* = 9.7 Hz), 7.88 br.s (1H, 3″-H), 8.20 br.s (1H, 5″-H). ^{13}C NMR spectrum, δ_C, ppm: 21.01 q [(C**H**$_3$)$_2$CH], 26.89 d [C**H**(CH$_3$)$_2$], 100.02 d (C^9), 111.47 s (C^{4a}), 114.90 d (C^6), 114.80 s (C^{3a}), 118.35 d (C^4), 121.86 d (C$^{2'}$), 131.23 s (C^3), 142.98 d (C$^{1'}$), 143.84 d (C^5), 152.26 s (C^{8a}), 152.40 d (C$^{5''}$), 155.20 d (C$^{3''}$), 155.96 s (C^{9a}), 160.29 s (C^7), 165.13 s (C^2). Found, %: C 66.88; H 4.01; N 13.02. $C_{18}H_{15}N_3O_3$. Calculated, %: C 67.28; H 4.71; N 13.08.

When the reaction was carried out as described in *a*, the corresponding *Z* isomer was detected among the products but was not isolated as individual substance. ^{1}H NMR spectrum of the *Z* isomer (from *Z*/*E* isomer mixture at a ratio of 1 : 4), δ, ppm: 1.08 d [6H, (C**H**$_3$)$_2$CH, *J* = 7.0 Hz], 3.34 [1H, C**H**(CH$_3$)$_2$], 6.35 d (1H, 6-H, *J* = 9.6 Hz), 6.96 s (1H, 9-H), 7.02 d (1H, 2′-H, *J* = 9.2 Hz), 7.28 d (1H, 1′-H, *J* = 9.2 Hz), 7.57 s (1H, 4-H), 7.62 d (1H, 5-H, *J* = 9.7 Hz), 7.95 br.s (1H, 3″-H), 8.39 br.s (1H, 5″-H).

2-Isopropyl-3-[(*E*)-2-(2-phenyl-1*H*-pyrrol-1-yl)-vinyl]-7*H*-furo[3,2-*g*]chromen-7-one (XV). Compound **III**, 250 mg (0.67 mmol), was dissolved in 5 ml of anhydrous DMF, 220 mg (1.3 mmol) of 2-phenyl-1-vinyl-1*H*-pyrrole (**XIII**), 2.2 mg (2 mol %) of $Pd(OAc)_2$, 32 mg (8 mol %) of (*o*-Tol)$_3$P, and 0.07 ml (1.3 equiv) of Et_3N were added under argon, and the mixture was heated for 8 h at 115°C (TLC), cooled, and poured onto a Petri dish for evaporation. The residue was subjected to column chromatography on silica gel using chloroform as eluent to isolate a fraction containing compound **XV** and traces of its *Z* isomer (according to the ^{1}H NMR data). Recrystallization from diethyl ether gave 110 mg (42%) of compound **XV** with mp 162–164°C. IR spectrum, ν, cm^{-1}: 3325, 3080, 3059, 2853, 1733, 1715, 1626, 1572, 1510, 1290, 1261, 1197, 1149, 1353, 1468, 1098, 1050, 1027, 919, 879, 850, 825, 800, 744, 700, 660. UV spectrum ($CHCl_3$), λ_{max}, nm (log ε): 254 (4.34), 299 (3.92), 310 (3.91), 349 (3.93). ^{1}H NMR spectrum, δ, ppm ($CDCl_3$–CD_3OD): 1.49 d [6H, (C**H**$_3$)$_2$CH, *J* = 7.0 Hz], 3.19 m [1H, C**H**(CH$_3$)$_2$], 6.26 d (1H, 6-H, *J* = 9.7 Hz), 6.64 d (1H, 2′-H, *J* = 12.8 Hz), 6.79 d.d (1H, 4″-H, *J* = 2.6, 2.2 Hz), 6.95 d (1H, 3″-H, *J* = 2.6 Hz), 6.98 d (1H, 1′-H, *J* = 12.8 Hz), 7.10 s (1H, 9-H), 7.11 d (1H, 5″-H, *J* = 2.2 Hz), 7.32 m (1H, *p*-H), 7.42 m (2H, *m*-H), 7.57 s (1H, 4-H), 7.61 d (2H, *o*-H, *J* = 7.0 Hz), 7.65 d (1H, 5-H, *J* = 9.7 Hz). ^{13}C NMR spectrum, δ_C, ppm: 29.58 q [(**C**H$_3$)$_2$CH], 34.40 d [**C**H(CH$_3$)$_2$], 100.68 d (C^9), 105.26 d (C$^{4''}$), 110.60 s (C^{4a}), 111.76 d (C$^{3''}$), 114.31 d (C^6), 115.09 s (C^{3a}), 118.45 d (C^4), 125.21 d (C^4), 129.06 d (C$^{2'}$), 129.69 d and 130.10 d (C^o), 130.22 d (C^p), 131.00 s (C^3), 132.43 d and 132.92 d (C^m), 133.71 s (C$^{2''}$), 144.44 d (C^5), 144.27 s (C^i), 147.08 d (C$^{1'}$), 150.63 s (C^{9a}), 156.61 s (C^2, C^{9a}), 160.15 s (C^7). Found, %: C 78.28; H 5.81; N 3.02. $C_{26}H_{21}NO_3$. Calculated, %: C 78.97; H 5.35; N 3.54.

X-Ray diffraction data for compound III. Monoclinic crystals. $C_{15}H_{11}F_3O_6S$. Unit cell parameters: *a* = 5.540(1), *b* = 16.060(3), *c* = 17.041(4) Å; β = 92.34(1)°, *V* = 1515.0(6) Å^3; space group $P2_1$; *Z* = 4; d_{calc} = 1.650 g/cm^3. Total of 11068 reflections were measured, 4898 of which were independent (R_{int} = 0.060). Corrections for absorption were introduced using SADABS program [17] which removed equivalent reflections measured at different orientations of the single crystal (transmission 0.59–0.97). The structure was solved by the direct method using SHELXS-97 software package [18] and was refined by the least-squares procedure in full-matrix anisotropic approximation using SHELXL-97 [18]. The positions of hydrogen atoms were calculated in each iteration cycle from the coordinates of the corresponding carbon atoms (riding model). Isotropic thermal parameters of all hydrogen atoms were equal to 1.2 U_{eq} (where U_{eq} is the equivalent thermal parameter of the corresponding carbon atom). The final divergence factors were *R* = 0.0608 (for 3686 reflections with $F > 4\sigma$) and wR_2 = 0.1494 (with respect to F^2); *S* = 1.07; 451 refined parameters; maximal and minimal electron density differences 0.45 and –0.49 *e*/Å^3. The coordinates of atoms, their thermal parameters, and geometric parameters of molecule **III** in crystal were deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 780428) and are available at *http:\\www.ccdc.cam.ac.uk/data_request/cif*.

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