Efficient Synthesis of Arylated Coumarins by Site-Selective Suzuki–Miyaura Cross-Coupling Reactions of the Bis(triflate) of 4-Methyl-5,7-dihydroxycoumarin

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Abstract: Arylated coumarins were prepared by site-selective Suzuki–Miyaura cross-coupling reactions of the bis(triflate) of 4-methyl-5,7-dihydroxycoumarin.

Key words: cyclization, domino reaction, 4-chloro-3-formylcoumarin, biaryl lactones, heterocycles

Coumarin and its derivatives are one of the important classes of heterocyclic compounds which occur in many natural products. For example, wedelolactone and other coumarins were isolated from the roots of *Hedysarum multijugum*, which is a plant in *Hedysarum Linn.* of the family *Leguminosae* used as a folk herbal drug in northwest China.[1] Several types of coumarins were isolated from plants, such as alternariol, umbelliferone (7-hydroxycoumarin), and others (Figure 1).[2] Coumarin derivatives are known to possess a wide range of biological activities, such as anti-HIV, antibiotic, antifungal, antibacterial, antiviral, anticancer, anticlotting, and anticoagulant activity.[3] They are widely used as additives in food, perfumes, agrochemicals, cosmetics, pharmaceuticals,[4] and in the preparations of insecticides, optical brightening agents, and dispersed fluorescent and laser dyes.[5]

Coumarins can be synthesized by various methods, such as Pechmann,[6] Perkin,[7] Knoevenagel,[8] and Wittig reactions.[9] Because of its operational simplicity and relatively inexpensive starting materials, the Pechmann reaction has been widely used for the synthesis of coumarin and its derivatives. This method involves the reaction of phenols with β-keto esters in the presence of acidic catalysts.[10–15] Transition-metal-catalyzed syntheses of coumarins have also been reported. Yang et al. reported the synthesis of 4-substituted coumarins by palladium-catalyzed cross-coupling reactions of 4-tosylcoumarins with terminal acetylenes and organozinc reagents.[16] A different approach to substituted coumarins relies on site-selective palladium-catalyzed cross-coupling reactions. Cross-coupling reactions of 3-bromo-4-trifloxycoumarin or 3-bromo-4-tosyloxycoumarin provide an efficient and facile route for the synthesis of 3,4-disubstituted coumarins.[17] Herein, we report a new and convenient synthesis of arylated coumarins by site-selective[18,19] Suzuki–Miyaura cross-coupling reactions of the bis(triflate) of 4-methyl-5,7-dihydroxycoumarin. The products reported herein are not readily available by other methods.

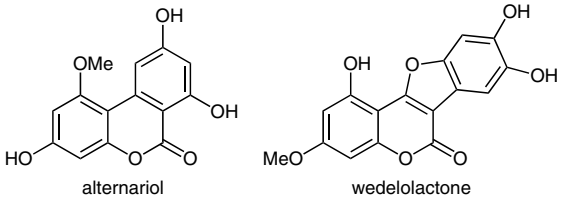
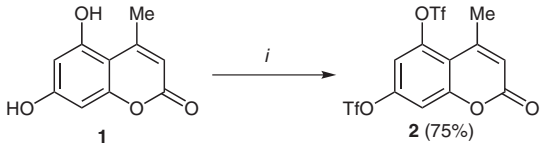


Figure 1 Natural products containing a benzo[*c*]chromen-6-one subunit

5,7-Dihydroxy-4-methylcoumarin was prepared by Pechman reaction of phloroglucinol (1,3,5-trihydroxybenzene) with ethyl acetoacetate in the presence of polyphosphoric acid.[20] The reaction of 5,7-dihydroxy-4-methylcoumarin (**1**) with triflic anhydride (2.4 equiv) afforded the bis(triflate) **2** in 75% yield (Scheme 1).[21]



Scheme 1 Synthesis of **2**. *Reagents and conditions*: (*i*) 1) **1** (1.0 equiv), Et_3N (4.0 equiv), CH_2Cl_2, 20 °C; 2) Tf_2O (2.4 equiv), –78 °C to 20 °C, 6 h.

The reaction of bis(triflate) **2** with two equivalents of arylboronic acids **3a–g** afforded the 5,7-diarylcoumarins **4a–g** in 70–86% yield (Scheme 2, Table 1).[22,23] The yields of the products derived from electron-rich boronic acids were higher than the yields of the products derived from electron-poor boronic acids.

The reaction of **2** with one equivalent of arylboronic acids **3a–e**,**h** afforded the 7-aryl-5-(trifluoromethylsulfonyloxy)coumarins **5a–f** in 60–80% yield (Scheme 3, Table 2).[22,24] The reactions proceeded with very good site-selectivity in favor of position 7. The yields of products derived from electron-rich boronic acids were again high-

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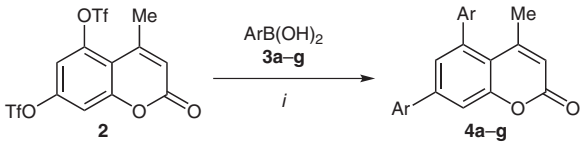


Scheme 2 Synthesis of **4a–g**. *Reagents and conditions*: (*i*) **2** (1.0 equiv), **3a–g** (2.0 equiv), K_3PO_4 (3.0 equiv), $Pd(PPh_3)_4$ (6 mol%), toluene–1,4-dioxane (1:1), 105 °C, 8 h.

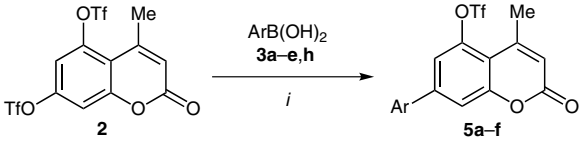
Table 1 Synthesis of **4a–g**

Entry	3	4	Ar	Yield of 4 (%)[a]
1	**3a**	**4a**	4-MeC_6H_4	86
2	**3b**	**4b**	3,5-MeC_6H_3	81
3	**3c**	**4c**	4-$MeOC_6H_4$	83
4	**3d**	**4d**	4-ClC_6H_4	77
5	**3e**	**4e**	4-FC_6H_4	74
6	**3f**	**4f**	4-$F_3CC_6H_4$	70
7	**3g**	**4g**	Ph	79

[a] Yields of isolated products.

er than the yields of the products derived from electron-poor boronic acids. During the optimization, it proved to be important to carry out the reaction at 70 °C instead of 105 °C (as for products **4a–g**). In some cases, a small amount of biscoupled product could be detected in the product mixture by TLC which could be easily separated by chromatography.

The structure of product **5b** was elucidated by 2D NMR spectroscopy (NOESY, COSY, HMBC, HSQC). A diagnostic NOESY correlation between hydrogen atoms H-6 and H-8 with the *ortho* protons of the 3,5-dimethylphenyl group was observed (Figure 2).



Scheme 3 Synthesis of **5a–f**. *Reagents and conditions*: (*i*) **2** (1.0 equiv), **3a–e**,**h** (1.0 equiv), K_3PO_4 (1.0 equiv), $Pd(PPh_3)_4$ (3 mol%), toluene, 70 °C, 8 h.

Table 2 Synthesis of **5a–f**

Entry	3	5	Ar	Yield of 5 (%)[a]
1	**3a**	**5a**	4-MeC_6H_4	80
2	**3b**	**5b**	3,5-MeC_6H_3	77
3	**3c**	**5c**	4-$MeOC_6H_4$	75
4	**3d**	**5d**	4-ClC_6H_4	60
5	**3e**	**5e**	4-FC_6H_4	63
6	**3h**	**5f**	4-EtC_6H_4	70

[a] Yields of isolated products.

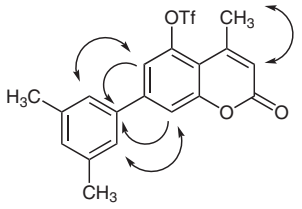
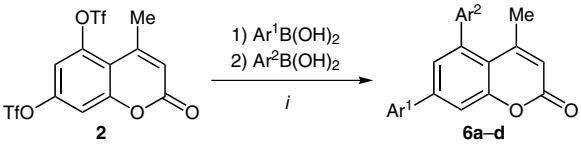


Figure 2 Important HMBC (single head arrows) and NOESY (double head arrows) correlations of **5b**

The one-pot reaction of **2** with two different arylboronic acids (sequential addition) afforded the 5,7-diarylcoumarins **6a–d** in 60–75% yield (Scheme 4, Table 3).[22,25] The first attack occurred at position 7. During the optimization it proved to be again important to carry out the first step at 70 °C to induce a good site-selectivity.



Scheme 4 Synthesis of **6a–d**. *Reagents and conditions*: (*i*) **2** (1.0 equiv), 1) $Ar^1B(OH)_2$ (1.0 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol%), toluene, 70 °C, 8 h; 2) $Ar^2B(OH)_2$ (1.0 equiv), K_3PO_4 (1.5 equiv), $Pd(PPh_3)_4$ (3 mol%), 1,4-dioxane, 105 °C, 8 h.

Table 3 Synthesis of **6a–d**

Entry	3	6	Ar^1	Ar^2	Yield of 6 (%)[a]
1	**3b**,**a**	**6a**	3,5-$Me_2C_6H_3$	4-MeC_6H_4	70
2	**3b**,**c**	**6b**	3,5-$Me_2C_6H_3$	4-FC_6H_4	60
3	**3a**,**d**	**6c**	4-MeC_6H_4	4-ClC_6H_4	62
4	**3c**,**a**	**6d**	4-$MeOC_6H_4$	4-MeC_6H_4	75

[a] Yields of isolated products.

The site-selective formation of products **5** and **6** can be explained by steric effects. The first attack occurs at the sterically less hindered position 7 (Figure 3). Position 5 and 7 can be considered similar with regard to their electron density. Therefore, electronic factors are unlikely to play a role.

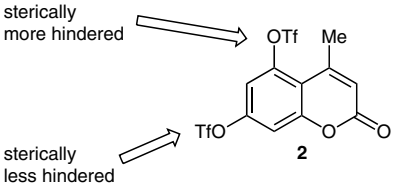


Figure 3 Possible explanation for the site-selectivity of the Suzuki reactions of **2**

In conclusion, we have reported a convenient synthesis of arylated coumarins by site-selective Suzuki–Miyaura cross-coupling reactions of the bis(triflate) of 4-methyl-5,7-dihydroxycoumarin. The selectivity is controlled by steric effects.

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References and Notes

(1) Wang, W.; Zhao, Y. Y.; Liang, H.; Jia, Q.; Chen, H. B. *J. Nat. Prod.* **2006**, *69*, 876.
(2) (a) Raistrick, H.; Stilkings, C. E.; Thomas, R. *Biochemistry* **1953**, *55*, 421. (b) Abaul, J.; Philogene, E.; Bourgeois, P. *J. Nat. Prod.* **1994**, *57*, 846.
(3) (a) Murakami, A.; Gao, G.; Omura, M.; Yano, M.; Ito, C.; Furukawa, H.; Takahashi, D.; Koshimizu, K.; Ohigashi, H. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 59. (b) Xia, Y.; Yang, Z.-Y.; Xia, P.; Hackl, T.; Hamel, E.; Mauger, A.; Wu, J.-H.; Lee, K.-H. *J. Med. Chem.* **2001**, *44*, 3932. (c) Itoigawa, M.; Ito, C.; Tan, H. T.-W.; Kuchide, M.; Tokuda, H.; Nishino, H.; Furukawa, H. *Cancer Lett.* **2001**, *169*, 15. (d) Yamaguchi, T.; Fukuda, T.; Ishibashi, F.; Iwao, M. *Tetrahedron Lett.* **2006**, *47*, 3755. (e) Yamamoto, Y.; Kurazono, M. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1626. (f) Kayser, O.; Kolodziej, H. *Planta Med.* **1997**, *63*, 508. (g) Wang, C. J.; Hsieh, Y. J.; Chu, C. Y.; Lin, Y. L.; Tseng, T. H. *Cancer Lett.* **2002**, *183*, 163.
(4) O'Kennedy, R.; Thornes, R. D. *Coumarins: Biology, Applications, and Mode of Action*; John Wiley and Sons: Chichester, **1997**.
(5) Murray, R. D. H.; Méndez, J.; Brown, S. A. *The Natural Coumarins: Occurrence, Chemistry, and Biochemistry*; Wiley: New York, **1982**.
(6) Sethna, S. M.; Phadke, R. *Org. React.* **1953**, *7*, 1.
(7) Donnelly, B. J.; Donnelly, D. M. X.; Sullivan, A. M. O. *Tetrahedron* **1968**, *24*, 2617.
(8) (a) Jones, G. *Org. React.* **1967**, *15*, 204. (b) Bigi, F.; Chesini, L.; Maggi, R.; Sartori, G. *J. Org. Chem.* **1999**, *64*, 1033.
(9) Yavari, I.; Hekmat-Shoar, R.; Zonuzi, A. *Tetrahedron Lett.* **1998**, *39*, 2391.
(10) Nadkarni, A. J.; Kudav, N. A. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **1981**, *20*, 719.
(11) Bose, D. S.; Rudradas, A. P.; Babu, M. H. *Tetrahedron Lett.* **2002**, *43*, 9195.
(12) Smitha, G.; Reddy, C. S. *Synth. Commun.* **2004**, *34*, 3997.
(13) Wang, L.; Xia, J.; Tian, H.; Qian, C.; Ma, Y. *Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem.* **2003**, *42*, 2097.
(14) Woods, L. L.; Sapp, J. *J. Org. Chem.* **1962**, *27*, 3703.
(15) Zagotto, G.; Gia, O.; Baccichetti, F.; Uriarte, E.; Palumbo, M. *Photochem. Photobiol.* **1993**, *58*, 486.
(16) Wu, J.; Liao, Y.; Yang, Z. *J. Org. Chem.* **2001**, *66*, 3642.
(17) Zhang, L.; Meng, T.; Fan, R.; Wu, J. *J. Org. Chem.* **2007**, *72*, 7279.
(18) For reviews of site-selective, palladium(0)-catalyzed cross-coupling reactions, see: (a) Schröter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245. (b) Schnürch, M.; Flasik, R.; Khan, A. F.; Spina, M.; Mihovilovic, M. D.; Stanetty, P. *Eur. J. Org. Chem.* **2006**, 3283. (c) Wang, R.; Manabe, K. *Synthesis* **2009**, 1405.
(19) For Suzuki–Miyaura reactions of bis(triflates) of benzene derivatives and other arenes, see for example: (a) Takeuchi, M.; Tuihiji, T.; Nishimura, J. *J. Org. Chem.* **1993**, *58*, 7388. (b) Sugiura, H.; Nigorikawa, Y.; Saiki, Y.; Nakamura, K.; Yamaguchi, M. *J. Am. Chem. Soc.* **2004**, *126*, 14858. (c) Akimoto, K.; Suzuki, H.; Kondo, Y.; Endo, K.; Akiba, U.; Aoyama, Y.; Hamada, F. *Tetrahedron* **2007**, *63*, 6887. (d) Akimoto, K.; Kondo, Y.; Endo, K.; Yamada, M.; Aoyama, Y.; Hamada, F. *Tetrahedron Lett.* **2008**, *49*, 7361. (e) Hosokawa, S.; Fumiyama, H.; Fukuda, H.; Fukuda, T.; Seki, M.; Tatsuta, K. *Tetrahedron Lett.* **2007**, *48*, 7305. (f) Nawaz, M.; Adeel, M.; Ibad, M. F.; Langer, P. *Synlett* **2009**, 2154. (g) Mahal, A.; Villinger, A.; Langer, P. *Synlett* **2010**, 1085. (h) Abid, O.-U.-R.; Ibad, M. F.; Nawaz, M.; Ali, A.; Sher, M.; Rama, N. H.; Villinger, A.; Langer, P. *Tetrahedron Lett.* **2010**, *51*, 1541. (i) Akrawi, O. A.; Hussain, M.; Langer, P. *Tetrahedron Lett.* **2011**, *52*, 1093. (j) Nawaz, M.; Khera, R. A.; Malik, I.; Ibad, F. A.; Villinger, A. M.; Langer, P. *Synlett* **2010**, 979.
(20) Kapil, R. S.; Joshi, S. S. *J. Indian Chem. Soc.* **1959**, *36*, 596.
(21) **4-Methyl-2-oxo-2*H*-chromene-5,7-diyl Bis(trifluoromethanesulfonate) (2)**
To a solution of 5,7-dihydroxycoumarin (**1**, 0.5 g, 2.60 mmol) in CH_2Cl_2 (30 mL) was added Et_3N (0.36 mL, 10.4 mmol) at r.t. under an argon atmosphere. After 10 min, Tf_2O (1.0 mL, 6.2 mmol) was added at –78 °C. The mixture was allowed to warm to 20 °C and stirred for 6 h. The reaction mixture was filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (flash silica gel, heptanes–EtOAc = 10:1) without aqueous workup to give **2** as a colourless solid (0.9 g, 75%), mp 131–132 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.56 (d, *J* = 1.3 Hz, CH_3), 6.32 (d, *J* = 1.3 Hz, 1 H), 7.19 (d, *J* = 2.5 Hz, 1 H), 7.28 (d, *J* = 2.5 Hz, 1 H). ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 21.9 (CH_3), 110.0, 110.6 (CH), 113.1 (C), 117.3 (q, $J_{F,C}$ = 320.0 Hz, CF_3), 117.6 (q, $J_{F,C}$ = 320.0 Hz, CF_3), 118.1 (CH), 144.8, 147.9, 148.5, 154.5 (C), 156.4 (CO). ^{19}F NMR (282.4, MHz): δ = –72.6, –72.2. IR (KBr): ν = 3181, 3111, 3084, 3065, 3020, 2935, 1795 (w), 1728, 1615 (s), 1566, 1547, 1530, 1476, 1454 (w), 1434, 1415 (s), 1379, 1359 (m), 1326, 1285 (w), 1244, 1235, 1218, 1202, 1132, 1124 (s), 1071 (m), 1052, 1006, 993 (s), 898, 878, 870 (m), 834, 796 (s), 771 (w), 759, 730, 707, 659 (m), 610, 589, 579 (s), 550, 538 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 456 (100) [M]$^+$, 323 (25), 295 (79), 231 (47), 203 (22), 162 (30), 134 (37). HRMS (EI, 70 eV): *m/z* calcd for $C_{12}H_6F_6O_8S_2$ [M]$^+$: 455.94028; found: 455.941352.
(22) **General Procedure for Suzuki–Miyaura Reactions**
A solution of K_3PO_4 (1.5 equiv per cross-coupling), $Pd(PPh_3)_4$ (3 mol% per cross-coupling step), and arylboronic acid **3** (1.1 equiv per cross-coupling) in the solvent indicated was stirred at the indicated temperature and for the indicated time. After cooling to 20 °C, distilled H_2O was added. The organic and the aqueous layers were separated, and the latter was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by column chromatography (flash silica gel, heptanes–EtOAc).
(23) **5,7-Bis(4-methoxyphenyl)-4-methyl-2*H*-chromen-2-one (4c)**
Starting with **2** (80 mg, 0.18 mmol), **3c** (48 mg, 0.35 mmol), $Pd(PPh_3)_4$ (6 mg, 3 mol%, 0.005 mmol), K_3PO_4 (111 mg, 0.525 mmol), and a toluene–1,4-dioxane mixture (1:1, 4 mL), **4c** was isolated by chromatography (flash silica gel, heptanes–EtOAc = 10:1) as a colourless solid (54 mg, 83%), mp 132–134 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.71 (d, *J* = 1.2 Hz, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 3.79 (s, 3 H,

OCH_3), 6.05 (d, J = 1.2 Hz, 1 H), 6.88 (m, 4 H), 7.14 (d, J = 8.7 Hz, 2 H), 7.22 (d, J = 2.0 Hz, 1 H), 7.42 (d, J = 2.0 Hz, 1 H), 7.50 (d, J = 8.8 Hz, 2 H). ^{13}C NMR (75.46 MHz, $CDCl_3$): δ = 24.0 (CH_3), 55.3, 55.4 (OCH_3), 113.4, 113.7, 114.5, 116.1 (CH), 117.0 (C), 126.2, 128.2, 130.3 (CH), 130.9, 134.3, 141.7, 142.5 153.9, 155.0, 159.4, 160.1 (C), 160.6 (CO). IR (KBr): ν = 3040, 2998, 2964, 2931, 2906, 2834, 1900, 1864, 1790 (w), 1722, 1715, 1597 (s), 1557, 1538 (m), 1514 (s), 1462, 1435 (m), 1514 (s), 1462, 1435 (m), 1393, 1378, 1351, 1309 (m), 1292, 1240 (s), 1195, 1177, 1138, 1110 (m), 1085 (w), 1032 (s), 1019 (m), 965, 942, 914, 894, 873, 849 (w), 830 (s), 793, 774, 738, 730, 718 (w), 706 (m), 672, 649, 629, 612, 603, 585, 546 (w). GC-MS (EI, 70 eV): *m/z* (%) = 372 (100) $[M]^+$, 371 (13), 344 (17), 329 (12). HRMS (EI, 70 eV): *m/z* calcd for $C_{24}H_{20}O_4$ $[M]^+$: 372.13561; found: 372.135278.

(24) **4-Methyl-2-oxo-7-(*p*-tolyl)-2*H*-chromen-5-yl Trifluoromethanesulfonate (4a)**

Starting with **2** (80 mg, 0.18 mmol), **3a** (24 mg, 0.18 mmol), $Pd(PPh_3)_4$ (6 mg, 3 mol%, 0.005 mmol), K_3PO_4 (55 mg, 0.26 mL), and toluene (3 mL), **4a** was isolated by chromatography (flash silica gel, heptanes–EtOAc = 10:1) as a colourless solid (55 mg, 80%), mp 135–136 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, CH_3), 2.56 (d, J = 1.2 Hz, 3 H, CH_3), 6.24 (d, J = 1.2 Hz, 1 H), 7.23 (d, J = 8.0 Hz, 2 H), 7.41 (d, J = 1.8 Hz, 1 H), 7.42 (d, J = 8.0 Hz, 2 H), 7.49 (d, J = 1.8 Hz, 1 H). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 21.2, 22.9 (CH_3), 112.3 (C), 115.0, 116.0, 117.7 (CH), 118.4 (q, $J_{F,C}$ = 318.8 Hz, CF_3), 126.8, 130.1 (CH), 134.2, 139.8, 144.8, 145.7, 149.6, 155.3 (C), 159.0 (CO). ^{19}F NMR (282.4, MHz): δ = –72.6. IR (KBr): ν = 3071, 3053, 3033, 2923, 2852, 1914, 1803 (w), 1735, 1613 (s), 1577, 1529, 1482, 1452 (w), 1424 (m), 1398 (s), 1386, 1364, 1292 (m), 1206, 1179, 1133 (s), 1089 (m), 1039, 926, 880, 869, 813, 787, 764, 758 (s), 735, 712, 703, 690 (w), 656 (m), 640, 633, 617 (w), 601, 574 (m), 548, 539 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 398 (100) $[M]^+$, 265 (16), 238 (17), 237 (85), 209 (34), 165 (32). HRMS (EI, 70 eV): *m/z* calcd for $C_{18}H_{13}F_3O_5S$ $[M]^+$: 398.04303; found: 398.04309.

(25) **7-(4-Methoxyphenyl)-4-methyl-5-(*p*-tolyl)-2*H*-chromen-2-one (6c)**

The reaction was carried out in a one-pot procedure with sequential addition of the boronic acids. Catalyst and base had to be added two times. Starting with **2** (80 mg, 0.175 mmol), **3c** (20 mg, 0.175 mmol), $Pd(PPh_3)_4$ (6 mg, 3 mol%, 0.005 mmol), K_3PO_4 (55 mg, 0.26 mmol), and then followed by toluene (3 mL), **3a** (23 mg, 0.18 mmol), $Pd(PPh_3)_4$ (6 mg, 3 mol%, 0.005 mmol), K_3PO_4 (55 mg, 0.26 mmol), and dioxane (3 mL), **6c** was isolated by chromatography (flash silica gel, heptanes–EtOAc = 10:1) as a colorless solid (47 mg, 75%), mp 256–258 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.73 (d, J = 1.2 Hz, 3 H, CH_3), 2.32 (s, 3 H, CH_3), 3.80 (s, 3 H, OCH_3), 6.09 (d, J = 1.2 Hz, 1 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.15–7.20 (m, 4 H), 7.26 (d, J = 2.0 Hz, 1 H), 7.45–7.49 (m, 3 H). ^{13}C NMR (75.47 MHz, $CDCl_3$): δ = 21.1, 24.1 (CH_3), 55.3 (OCH_3), 113.4, 114.1, 116.3 (CH_3), 117.3 (C), 126.5, 126.9, 129.7, 130.3 (CH), 134.3, 135.6, 138.6, 141.7, 142.8, 153.9, 154.9, 159.4 (C), 160.5 (CO). IR (KBr): ν = 3029, 2927, 2852, 2836 (w), 1725 (s), 1642 (w), 1599 (s), 1574, 1536 (w), 1510 (s), 1464, 1439, 1391, 1379, 1354, 1286 (m), 1243 (s), 1191, 1176, 1137 (s), 1108, 1084 (w), 1032 (s), 1017 (w), 963 (s), 893, 875, 853, 834 (w), 816 (s), 795, 778, 726, 714, 672, 648 (w), 613, 582, 555 (w) cm^{-1}. GC-MS (EI, 70 eV): *m/z* (%) = 356 (100) $[M]^+$, 355 (11), 328 (26). HRMS (EI, 70 eV): *m/z* calcd for $C_{24}H_{20}O_3$ $[M]^+$: 356.14070; found: 356.140927.

