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Suzuki reactions on chloropyridazinones: an easy approach towards arylated 3(2*H*)-pyridazinones

Bert U. W. Maes,[a,b] Omar R'kyek,[a] Janez Košmrlj,[c] Guy L. F. Lemière,[a,*] Eddy Esmans,[a] Jef Rozenski,[d] Roger A. Dommisse[a] and Achiel Haemers[b]

[a]*Department of Chemistry, University of Antwerp (RUCA), Groenenborgerlaan 171, B-2020 Antwerpen, Belgium*
[b]*Department of Medicinal Chemistry, University of Antwerp (UIA), Universiteitsplein 1, B-2610 Antwerpen, Belgium*
[c]*Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, SI-1000 Ljubljana, Slovenia*
[d]*Faculty of Pharmaceutical Sciences, REGA Institute, Katholieke Universiteit Leuven, Minderbroedersstraat 10, B-3000 Leuven, Belgium*

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Abstract—The synthesis of 4-aryl-5-methoxy-, 5-aryl-4-methoxy- and 4,5-diaryl-3(2*H*)-pyridazinones via Suzuki palladium-catalysed cross-coupling reactions with the corresponding chloro-3(2*H*)-pyridazinones is described.

2,4,5-Trisubstituted-3(2*H*)-pyridazinones are well-known compounds in agrochemical and pharmaceutical research. One of the oldest representatives of the former is Chloridazon (5-amino-4-chloro-2-phenyl-3(2*H*)-pyridazinone).[1] This commercial herbicide developed by BASF researchers is still extensively used for weed control in sugar beet and red table beet cultivation. Since the marketing of Chloridazon (Pyramin®,1964) a large number of patents and papers has been published dealing with the synthesis and pesticidal activity of 2,4,5-trisubstituted-3(2*H*)-pyridazinones.[2–5] Recently Pyramite™, a 2-*tert*-butyl-5-(4-*tert*-butylbenzylthio)-4-chloro-3(2*H*)-pyridazinone (Pyridaben)-containing composition, has been commercialized.[1,2m] This selective contact miticide/insecticide controls pests in apple, pear and almond orchards. Besides the agrochemical applications of 2,4,5-trisubstituted-3(2*H*)-pyridazinones several interesting pharmaceutical activities (e.g. analgesic, anti-inflammatory, anticonvulsant, antitumour, antiviral, antibacterial, antifungal) are reported.[3–7] An important example is Emorfazone (4-ethoxy-2-methyl-5-morpholino-3(2*H*)-pyridazinone). This analgesic anti-inflammatory agent has been launched as Pentoil, Pentoyl and Nandron.[6]

Since the 2,4,5-trisubstituted-3(2*H*)-pyridazinone skeleton is so attractive from an agrochemical and pharmaceutical point of view we started a research project dealing with the synthesis of hitherto less-studied classes. To the best of our knowledge only a few articles and patents deal with the synthesis of 4-aryl-, 5-aryl- and 4,5-diaryl-2,4,5-trisubstituted-3(2*H*)-pyridazinones.[5,8–11] Therefore we searched for a new, short, experimentally easy and generally applicable method for the synthesis of arylated 3(2*H*)-pyridazinones starting from cheap readily available starting materials. We found that the Suzuki[12–15] cross-coupling reaction of arylboronic acids and chloro-3(2*H*)-pyridazinones works smoothly (Tables 1, 2 and 3). The fact that a C—Cl bond undergoes oxidative addition is not self-evident since it is well known that the oxidative insertion of palladium into this bond requires a much higher energy than in the case of a C—OTf, C—Br or C—I bond.[13,14] Recently new ligands for the palladium catalyst were developed which make Suzuki palladium-catalysed cross-coupling reactions possible with electron neutral and rich chlorobenzene derivatives.[16–21] In this case the use of strongly electron donating and sterically bulky ligands seem to be essential. However, it is also known that the introduction of electron withdrawing substituents onto or the incorporation of nitrogen atoms into the benzene ring decreases the required energy for oxidative addition. When this energy is sufficiently decreased palladium catalysts containing ligands which are less electron donating are able to insert into the C—Cl bond.[22–30] We found that chloro-3(2*H*)-pyridazinones undergo oxidative addition with commonly used tetrakis triphenylphosphine palladium, and we present here our results on palladium-catalysed arylations of chloro-3(2*H*)-pyridazinones with this complex as the catalyst.[11,31]

The reason that so much interest is shown by researchers from academic and industrial laboratories with regard to the use of chlorinated compounds in Suzuki palladium-catalysed cross-coupling reactions is obvious: the chlorinated compounds are readily available and less expensive

Keywords: palladium and compounds; Suzuki reactions; pyridazinones.
* Corresponding author. Tel.: +32-3-21-80-226; fax: +32-3-21-80-233; e-mail: lemiere@ruca.ua.ac.be

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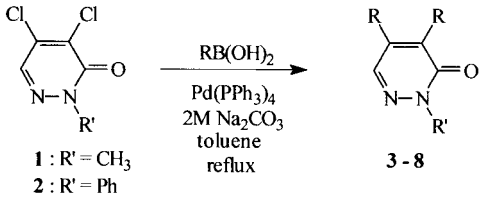
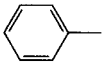
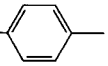
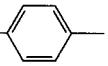
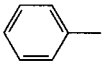
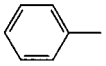
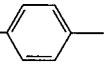
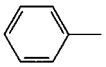
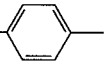
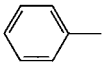
PII: S0040-4020(00)01100-5

Table 1.



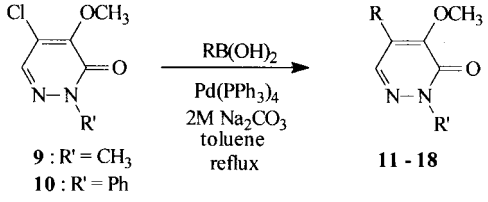
1 : R' = CH_3
2 : R' = Ph

3 - 8

Reaction product	R	R'	Yield (%)
3		CH_3	98
4	CH_3O 	CH_3	97
5	F 	CH_3	100
6			97
7	CH_3O 		87
8	F 		100

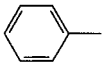
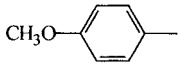
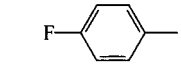
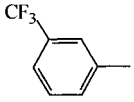
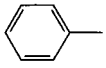
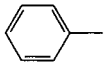
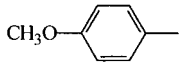
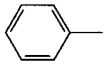
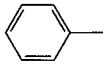
1 or **2** (2.55 mmol), boronic acid (7.65 mmol), $Pd(PPh_3)_4$ (3 mol%), Na_2CO_3 (2 M, 4 mL).

Table 2.



9 : R' = CH_3
10 : R' = Ph

11 - 18

Reaction product	R	R'	Yield (%)
11		CH_3	100
12	CH_3O 	CH_3	100
13	F 	CH_3	100
14	CF_3 	CH_3	100
15		CH_3	85
16			100
17	CH_3O 		100
18			100

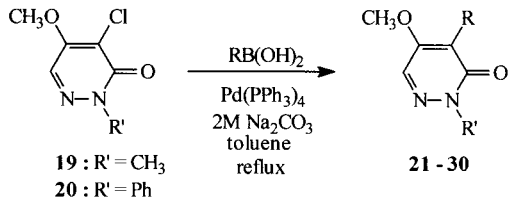
9 or **10** (1.28 mmol), boronic acid (1.92 mmol), $Pd(PPh_3)_4$ (3 mol%), Na_2CO_3 (2 M, 1.4 mL).

than the corresponding bromo or iodo analogues. Especially, the availability of chlorinated 1,2-diazines is excellent. The preference for the Suzuki reaction above other palladium-catalysed cross-coupling reactions is not coincidental. It possesses the advantage that non-toxic, easily removable boron-containing by-products are generated. On a laboratory scale the cost and environmental factor may seem less relevant but in large-scale industrial syntheses they are critical.

Suzuki reaction of 2-methyl- and 2-phenyl-4,5-dichloro-3(2*H*)-pyridazinone (**1**, **2**) with 3 equivalents of several arylboronic acids gave 2-methyl- and 2-phenyl-4,5-diaryl-3(2*H*)-pyridazinones in very good yields (Table 1). Attempts to perform selective arylations on **1** and **2** using only one equivalent of boronic acid failed. DCI-MS spectra of the reaction mixtures showed the formation of mono- as well as diaryl-3(2*H*)-pyridazinones. When a strong electron donating group such as a methoxy group is present on the 3(2*H*)-pyridazinone skeleton (**9**, **10**, **19**, **20**) excellent results were obtained (Tables 2 and 3). Even 4-chloro-5-methoxy-2-methyl-3(2*H*)-pyridazinone (**19**), in which the chlorine atom is surrounded by two groups at the *ortho* position, gave Suzuki reaction with *ortho*-substituted boronic acids. Only in the case of the synthesis of 4-(2,4-dichlorophenyl)-5-methoxy-2-methyl-3(2*H*)-pyridazinone (**28**) the standard conditions (1,5 equivalents of boronic acid per chlorine atom, 3 mol% of Pd catalyst, 2 M Na_2CO_3) used for all syntheses, including the synthesis of 5-methoxy-2-methyl-4-(2-methylphenyl)-3(2*H*)-pyridazinone (**27**), produced an incomplete reaction even after two days of reflux. Attempts to use solid bases (K_3PO_4 in dioxane, KO*t*Bu in toluene or DME, KOH or Cs_2CO_3 in toluene) instead of aqueous solutions in refluxing toluene, dioxane or DME were unsuccessful. Since stronger bases are known to accelerate the Suzuki cross-coupling reaction, $Ba(OH)_2{\cdot}(H_2O)_8$ was used as a base instead of Na_2CO_3.[32] These conditions gave complete consumption of **19** but with only a 21% yield. We found that the low yield of **28** is due to a competitive decomposition of starting material (**19**) by the strong aqueous base. Refluxing **28** for 24 h in a two-phase system of aqueous $Ba(OH)_2$ and toluene gave nearly complete recovery of **28**, while treatment of **19** under the same conditions gave complete decomposition of **19**. Finally, we observed that increasing the amount of 2,4-dichlorobenzeneboronic acid from 1.5 to 2.5 equivalents gives a complete reaction in 15 h.

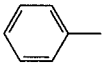
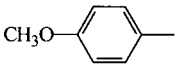
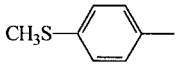
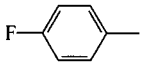
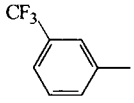
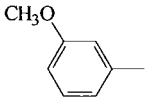
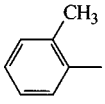
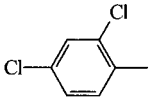
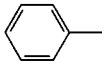
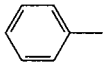
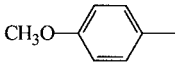
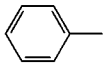
Since chloro-3(2*H*)-pyridazinones are cheap and easily accessible we believe that we have developed a simple

Table 3.



19 : R' = CH_3
20 : R' = Ph

21 - 30

Reaction product	R	R'	Yield (%)
21		CH_3	100
22		CH_3	100
23		CH_3	100
24		CH_3	100
25		CH_3	97
26		CH_3	100
27		CH_3	100
28		CH_3	90
29			100
30			94

19 or **20** (1.28 mmol), boronic acid (**21**–**27**, **29**–**30**: 1.92 mmol; **28**: 3.2 mmol), $Pd(PPh_3)_4$ (3 mol%), Na_2CO_3 (2 M, 1.4 mL).

and powerful method with broad application for the synthesis of arylated 3(2*H*)-pyridazinones. Future research towards the application of this methodology to the synthesis of hitherto less easily accessible or unknown carbon-substituted 3(2*H*)-pyridazinones is in progress.

1. Experimental

^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Varian Unity 400 or a Bruker 400 spectrometer in DMSO-d_6, with TMS as the internal standard. Chemical shifts are given in ppm and *J* values in Hz. The numbering used for the assignment of NMR signals is as follows: pyridazinone ring, simple figures; 4-substituents, primed figures; 5-substituents, double primed figures; and *N*-substituents, triple primed figures. LRMS were performed on a Quattro II triple quadrupole mass spectrometer (Micromass, Manchester, UK) equipped with a standard electrospray ionization (ESI) interface. Samples were infused in a AcOH–2% MeOH (20:80) mixture at 50 μL/min. The capillary voltage was set at 3.74 V, the cone voltage at 40 V. Product ions were generated in the collision cell, using 3.5×10^{-3} mbar Ar as a collision gas and a collision energy of 25 eV. HRMS values were recorded on a quadrupole-time of flight mass spectrometer (QTof2, Micromass, Manchester, UK) equipped with a standard electrospray ionization (ESI) interface. Samples were infused in a 2-propanol–water (1:1) mixture at 3 μL/min. IR spectra were obtained as potassium bromide pellets with a Bruker vector 22 spectrometer. Melting points were determined on a Büchi B-545 apparatus and are uncorrected. 4,5-Dichloro-2-methyl-3(2*H*)-pyridazinone (**1**) (Avocado and Lancaster), 4,5-dichloro-2-phenyl-3(2*H*)-pyridazinone (**2**) (Avocado), 4-chloro-5-methoxy-2-methyl-3(2*H*)-pyridazinone (**19**) (Avocado) and $Pd(PPh_3)_4$ (Acros) were obtained from commercial sources. The boronic acids were purchased from Aldrich and Lancaster. Flash column chromatography was performed on Kieselgel 60 (Merck), 0.040–0.063 mm.

1.1. General procedure for the synthesis of compounds 3–8 via the Suzuki cross-coupling reaction

A mixture of 2-substituted-4,5-dichloro-3(2*H*)-pyridazinone (**1** or **2**, 2.55 mmol), boronic acid (7.65 mmol), $Pd(PPh_3)_4$ (0.090 g, 0.078 mmol), toluene (15 mL) and aqueous Na_2CO_3 (4 mL, 2 M) was flushed with N_2 for 5 min under magnetic stirring. The reaction mixture was stirred and heated under reflux (temperature of oil bath=120°C) under a N_2 atmosphere until starting material had disappeared as judged by TLC and/or DCI-MS. After cooling, the reaction mixture was evaporated to dryness under reduced pressure. EtOAc (80 mL) was added and the suspension was placed in an ultrasonic bath for a few minutes. The mixture was filtered, washed thoroughly with EtOAc (200 mL) and the filtrate evaporated to dryness under reduced pressure. The residue was purified by flash column chromatography on silica gel.

The following compounds were prepared in this manner.

1.1.1. 2-Methyl-4,5-diphenyl-3(2*H*)-pyridazinone (3). Yield: 98%; eluent for flash column chromatography: heptane–EtOAc (7:3); mp 172°C (white solid); ν_{max}: 3061, 2939, 1630, 1590, 1445, 1342, 1302, 1016, 765, 700 cm^{-1}; δ_H: 8.00 (s, 1H, H-6), 7.30–7.23 (m, 6H, H-3′, H-4′, H-3″, H-4″), 7.12–7.18 (m, 4H, H-2′, H-2″), 3.75 (s, 3H, NCH_3); δ_C: 159.31 (C-3), 140.44 (C-5), 137.74 (C-6), 135.99 (C-4), 134.75 (C-1″), 132.98 (C-1′), 130.18 (C-2′), 128.98 (C-2″), 128.36 (C-4″), 128.26 (C-3″), 127.85 (C-4′), 127.54 (C-3′), 40.11 (NCH_3); LRMS (ESI): 263 (100%), 178; HRMS (ESI) for $C_{17}H_{15}N_2O$ $[M+H]^+$: calcd 263.1184, found 263.1203; $C_{17}H_{14}N_2O$: calcd C 77.84, H 5.38, N 10.68, found C 77.59, H 5.40, N 10.79.

1.1.2. 4,5-Bis(4-methoxyphenyl)-2-methyl-3(2*H*)-pyridazinone (4). Yield: 97%; eluent for flash column chromatography: heptane–EtOAc (6:4); mp 169°C (yellow solid); ν_{max}: 3045, 2939, 2842, 1630, 1608, 1514, 1503, 1297, 1251, 1172, 1024, 840, 820, 561 cm^{-1}; δ_H: 7.95 (s, 1H, H-6), 7.11 (d, J=8.9 Hz, 2H, H-2″), 7.09 (d, J=8.9 Hz, 2H, H-2′), 6.86 (d, J=8.9 Hz, 2H, H-3″), 6.83 (d, J=8.9 Hz, 2H, H-3′), 3.73 (2×s, 6H, 2×OCH_3), 3.72 (s, 3H, NCH_3); δ_C: 159.56 (C-3), 159.18 (C-4″), 158.76 (C-4′), 139.51 (C-5), 137.97 (C-6), 134.83 (C-4), 131.69 (C-2′), 130.41 (C-2″), 127.09 (C-1″), 125.12 (C-1′), 113.88 (C-3″), 113.11 (C-3′), 55.05 and 54.93 (4′-OCH_3 and 4″-OCH_3), 40.02 (NCH_3); LRMS (ESI): 323 (100%), 307, 279; HRMS (ESI) for $C_{19}H_{19}N_2O_3$ $[M+H]^+$: calcd 323.1395, found 323.1376; $C_{19}H_{18}N_2O_3$: calcd C 70.79, H 5.63, N 8.69, found C 70.81, H 5.55, N 8.40.

1.1.3. 4,5-Bis(4-fluorophenyl)-2-methyl-3(2*H*)-pyridazinone (5). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (96:4); mp 188°C (white solid); ν_{max}: 3060, 3044, 1629, 1598, 1505, 1297, 1227, 1171, 849, 831, 550 cm^{-1}; δ_H: 8.00 (s, 1H, H-6), 7.21 (dd, J_{HH}=9.0 Hz, J_{HF}=5.5 Hz, 2H, H-2″), 7.18 (dd, J_{HH}=9.0 Hz, J_{HF}=5.5 Hz, 2H, H-2′), 7.14 (t, J_{HH}=J_{HF}=9.0 Hz, 2H, H-3″), 7.10 (t, J_{HH}=J_{HF}=9.0 Hz, 2H, H-3′), 3.73 (s, 3H, NCH_3); δ_C: 159.24 (C-3), 139.70 (C-5), 137.66 (C-6), 135.14 (C-4), 132.50 (d, J_{CF}=8.4 Hz, C-2′), 131.33 (d, J_{CF}=8.4 Hz, C-2″), 131.04 (d, J_{CF}=3.0 Hz, C-1″), 129.10 (d, J_{CF}=3.8 Hz, C-1′), 115.41 (d, J_{CF}=21.3 Hz, C-3″), 114.67 (d, J_{CF}=21.4 Hz, C-3′), 40.12 (NCH_3); LRMS (ESI): 299 (100%); HRMS (ESI) for $C_{17}H_{13}F_2N_2O$ $[M+H]^+$: calcd 299.0995, found 299.1017; $C_{17}H_{12}F_2N_2O$: calcd C 68.45, H 4.05, N 9.39, found C 68.30, H 4.18, N 9.28.

1.1.4. 2,4,5-Triphenyl-3(2*H*)-pyridazinone (6). Yield: 97%; eluent for flash column chromatography: CH_2Cl_2–heptane (8:2); mp 181°C (white solid); ν_{max}: 3057, 1640, 1590, 1489, 1300, 1134, 761, 698 cm^{-1}; δ_H: 8.19 (s, 1H, H-6), 7.64 (br d, J=8 Hz, 2H, H-2‴), 7.53 (br t, J=8 Hz, 2H, H-3‴), 7.44 (br t, J=8 Hz, 1H, H-4‴), 7.19–7.33 (m, 10H, 4-Ph and 5-Ph); δ_C: 158.97 (C-3), 141.78 (C-1‴), 140.29 (C-5), 138.84 (C-6), 137.46 (C-4), 134.59 (C-1″), 132.89 (C-1′), 130.27 (C-2′), 129.01 (C-2″), 128.51 (C-3‴ and C-4″), 128.32 (C-3″), 127.96 (C-4′), 127.90 (C-4‴), 127.56 (C-3′), 125.58 (C-2‴); LRMS (ESI): 325 (100%), 191; HRMS (ESI) for $C_{22}H_{17}N_2O$ $[M+H]^+$: calcd 325.1340, found 325.1383; $C_{22}H_{16}N_2O$: calcd C 81.46, H 4.97, N 8.64, found C 81.23, H 5.01, N 8.59.

1.1.5. 4,5-Bis(4-methoxyphenyl)-2-phenyl-3(2*H*)-pyridazinone (7). Yield: 87%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (98:2); mp 174°C (white solid); ν_{max}: 3015, 2956, 2927, 2833, 1646, 1602, 1500, 1292, 1248, 1179, 1030, 820, 700, 615, 559, 541 cm^{-1}; δ_H: 8.13 (s, 1H, H-6), 7.61 (br d, J=7.9 Hz, 2H, H-2‴), 7.51 (br t, J=7.7 Hz, 2H, H-3‴), 7.42 (br t, J=7.3 Hz, 1H, H-4‴), 7.17 (d, J=8.6 Hz, 2H, H-2″), 7.15 (d, J=8.6 Hz, 2H, H-2′), 6.88 (d, J=8.6 Hz, 2H, H-3″), 6.83 (d, J=8.6 Hz, 2H, H-3′), 3.73 (s, 3H, 4″-OCH_3), 3.72 (s, 3H, 4′-OCH_3); δ_C: 159.36 (C-4″), 159.27 (C-3), 158.90 (C-4′), 141.92 (C-1‴), 139.40 (C-5), 139.16 (C-6), 136.21 (C-4), 131.84 (C-2′), 130.58 (C-2″), 128.53 (C-3‴), 127.85 (C-4‴), 126.92 (C-1″), 125.66 (C-2‴), 125.07 (C-1′), 113.98 (C-3″), 113.20 (C-3′), 55.12 (4″-OCH_3), 54.98 (4′-OCH_3); LRMS (ESI): 385 (100%); HRMS (ESI) for $C_{24}H_{21}N_2O_3$ $[M+H]^+$: calcd 385.1552, found 385.1613; $C_{24}H_{20}N_2O_3$: calcd C 74.98, H 5.24, N 7.29, found C 75.05, H 5.33, N 7.37.

1.1.6. 4,5-Bis(4-fluorophenyl)-2-phenyl-3(2*H*)-pyridazinone (8). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (99:1); mp 179°C (white solid); ν_{max}: 3076, 3042, 1639, 1601, 1504, 1228, 1133, 847, 759, 691, 616, 523 cm^{-1}; δ_H: 8.19 (s, 1H, H-6), 7.63 (br d, J=7.7 Hz, 2H, H-2‴), 7.52 (br t, J=7.7 Hz, 2H, H-3‴), 7.43 (br t, J=7.7 Hz, 1H, H-4‴), 7.29 (dd, J_{HH}=8.6 Hz J_{HF}=5.7 Hz, 2H, H-2″), 7.26 (dd, J_{HH}=8.6 Hz, J_{HF}=5.7 Hz, 2H, H-2′), 7.18 (t, J_{HF}=8.6 Hz, 2H, H-3″), 7.12 (t, J_{HH}=J_{HF}=8.6 Hz, 2H, H-3′); δ_C: 162.03 (d, J_{CF}=246.9 Hz, C-4″), 161.68 (d, J_{CF}=245.7 Hz, C-4′), 158.95 (C-3), 141.72 (C-1‴), 139.58 (C-5), 138.77 (C-6), 136.64 (C-4), 132.62 (d, J_{CF}=8.3 Hz, C-2′), 131.44 (d, J_{CF}=9.1 Hz, C-2″), 130.89 (d, J_{CF}=3.1 Hz, C-1″), 129.05 (d, J_{CF}=3.0 Hz, C-1′), 128.56 (C-3‴), 127.98 (C-4‴), 125.57 (C-2‴), 115.49 (d, J_{CF}=22.1 Hz, C-3″), 114.72 (d, J_{CF}=21.3 Hz, C-3′); LRMS (ESI): 361 (100%); HRMS (ESI) for $C_{22}H_{15}F_2N_2O$ $[M+H]^+$: calcd 361.1152, found 361.1167; $C_{22}H_{14}F_2N_2O$: calcd C 73.33, H 3.92, N 7.77, found C 73.29, H 3.99, N 7.63.

1.2. Synthesis of 2-methyl- and 2-phenyl-5-chloro-4-methoxy-3(2*H*)-pyridazinone (9, 10)[33]

1.2.1. 5-Chloro-4-methoxy-2-methyl-3(2*H*)-pyridazinone (9). To a magnetically stirred solution of 4,5-dichloro-2-methyl-3(2*H*)-pyridazinone (4.47 mmol, 0.8 g) in 20 mL of dry dioxane was added 1 mL of a 4.86 M $NaOCH_3$ solution. The solution was stirred at room temperature for 1 h and then poured into 100 mL H_2O/150 mL CH_2Cl_2. The organic layer was separated and dried over $MgSO_4$ and evaporated to dryness. The residue was purified by flash column chromatography: CH_2Cl_2–EtOAc (99:1); yield: 70–80% (sublimation-sensitive product); mp 86°C (white solid); ν_{max}: 3076, 3034, 2946, 2843, 1633, 1593, 1300, 1059, 960, 621, 500 cm^{-1}; δ_H: 7.99 (s, 1H, H-6), 4.14 (s, 3H, OCH_3), 3.64 (s, 3H, NCH_3); δ_C: 156.47 (C-3), 150.42 (C-4), 136.78 (C-6), 122.32 (C-5), 60.00 (OCH_3), 39.51 (NCH_3); LRMS (ESI): 175/177, product ions from 175: 162, 134, 119, 117, 115, 106 (100%), 105, 99, 91, 83, 78, 73; HRMS (ESI) for $C_6H_8ClN_2O_2$ $[M+H]^+$: calcd 175.0274, found 175.0287; $C_6H_7ClN_2O_2$: calcd C 41.28, H 4.04, N 16.05, found C 41.05, H 4.24, N 15.99.

1.2.2. 5-Chloro-4-methoxy-2-phenyl-3(2*H*)-pyridazinone (10). To a magnetically stirred solution of 4,5-dichloro-2-phenyl-3(2*H*)-pyridazinone (4.47 mmol, 1.08 g) in 20 mL of dry dioxane was added 1 mL of a 4.86 M $NaOCH_3$ solution. The solution was stirred at room temperature for 1 h and then poured into 100 mL H_2O/150 mL CH_2Cl_2. The organic layer was separated and dried over $MgSO_4$ and evaporated to dryness. The residue was purified by flash column chromatography: CH_2Cl_2; yield: 72%; mp 117°C (white solid); ν_{max}: 3066, 2961, 1639, 1608, 1400, 1299, 1147, 949, 757, 685, 569 cm^{-1}; δ_H: 8.16 (s, 1H, H-6), 7.50–7.53 (m, 5H, NPh), 4.17 (s, 3H, OCH_3); δ_C: 156.22 (C-3), 151.37 (C-4), 140.87 (C-1‴), 137.74 (C-6), 128.58 (C-3‴), 128.26 (C-4‴), 125.71 (C-2‴), 122.16 (C-5), 60.21

(OCH_3); LRMS (ESI): 237/239, product ions from 237: 221, 194, 165, 119, 103, 77 (100%); HRMS (ESI) for $C_{11}H_{10}ClN_2O_2$ $[M+H]^+$: calcd 237.0430, found 237.0381; $C_{11}H_9ClN_2O_2$: calcd C 55.83, H 3.83, N 11.84, found C 55.92, H 3.85, N 11.79.

1.3. General procedure for the synthesis of compounds 11–18 and 21–30 via the Suzuki cross-coupling reaction

A mixture of 2-substituted-3(2*H*)-pyridazinone (**9**, **10**, **19** or **20**, 1.28 mmol), boronic acid (1.92 mmol) (for the synthesis of **28**, 3.2 mmol 2,4-dichlorobenzeneboronic acid was used), $Pd(PPh_3)_4$ (0.045 g, 0.039 mmol), toluene (8 mL) and Na_2CO_3 (1.4 mL, 2 M) was flushed with N_2 for 5 min under magnetic stirring. The reaction mixture was stirred and heated under reflux (temperature of oil bath=120°C) under a N_2 atmosphere until starting material had disappeared as judged by TLC and/or DCI-MS. After cooling, the reaction mixture was evaporated to dryness under reduced pressure. EtOAc (40 mL) was added and the suspension was placed in an ultrasonic bath for a few minutes. The mixture was filtered, washed thoroughly with EtOAc (100 mL) and the filtrate evaporated to dryness under reduced pressure. The residue was purified by flash column chromatography on silica gel.

The following compounds were prepared in this manner.

1.3.1. 4-Methoxy-2-methyl-5-phenyl-3(2*H*)-pyridazinone (11). Yield: 100%; eluent for flash column chromatography: heptane–EtOAc (7:3); mp 78°C (white solid); ν_{max}: 3059, 3023, 2982, 2942, 1653, 1600, 1449, 1314, 1003, 923, 751, 697, 509 cm^{-1}; δ_H: 7.99 (s, 1H, H-6), 7.61 (br d, J=8 Hz, 2H, H-2″), 7.56–7.49 (m, 3H, H-3″ and H-4″), 4.04 (s, 3H, OCH_3), 3.75 (s, 3H, NCH_3); δ_C: 157.40 (C-3), 150.24 (C-4), 137.60 (C-6), 131.75 (C-1″), 128.71 (C-2″), 128.71 (C-4″), 128.61 (C-5), 128.39 (C-3″), 59.42 (OCH_3), 39.51 (NCH_3); LRMS (ESI): 217, 201 (100%), HRMS (ESI) for $C_{12}H_{13}N_2O_2$ $[M+H]^+$: calcd 217.0976, found 217.0981; $C_{12}H_{12}N_2O_2$: calcd C 66.65, H 5.59, N 12.96, found C 66.66, H 5.63, N 12.88.

1.3.2. 4-Methoxy-5-(4-methoxyphenyl)-2-methyl-3(2*H*)-pyridazinone (12). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (9:1); mp 104°C (white solid); ν_{max}: 3053, 3009, 2978, 2939, 2843, 1641, 1606, 1515, 1294, 1250, 1192, 1031, 923, 844, 608 cm^{-1}; δ_H: 7.95 (s, 1H, H-6), 7.56 (d, J=9 Hz, 2H, H-2″), 7.05 (d, J=9 Hz, 2H, H-3″), 3.97 (s, 3H, 4-OCH_3), 3.81 (s, 3H, 4″-OCH_3), 3.69 (s, 3H, NCH_3); δ_C: 159.70 (C-4″), 157.54 (C-3), 149.81 (C-4), 137.68 (C-6), 130.26 (C-2″), 128.48 (C-5), 123.81 (C-1″), 113.99 (C-3″), 59.31 (4-OCH_3), 55.19 (4″-OCH_3), 39.40 (NCH_3); LRMS (ESI): 247, 232 (100%), 231, 217, 132; HRMS (ESI) for $C_{13}H_{15}N_2O_3$ $[M+H]^+$: calcd 247.1082, found 247.1113; $C_{13}H_{14}N_2O_3$: calcd C 63.40, H 5.73, N 11.38, found C 63.69, H 5.77, N 11.40.

1.3.3. 5-(4-fluorophenyl)-4-methoxy-2-methyl-3(2*H*)-pyridazinone (13). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (94:6); mp 98°C (white solid); ν_{max}: 3067, 3043, 2948, 2851, 1640, 1605, 1514, 1319, 1235, 1161, 999, 926, 826, 739, 602, 494 cm^{-1}; δ_H: 7.94 (s, 1H, H-6), 7.62 (dd, J_{HH}=9 Hz J_{HF}=5.5 Hz, 2H, H-2″), 7.31 (t, J_{HH}=J_{HF}=9 Hz, 2H, H-3″), 3.99 (s, 3H, OCH_3), 3.68 (s, 3H, NCH_3); δ_C: 162.20 (d, J_{CF}=247.2 Hz, H-2″), 157.39 (C-3), 150.26 (C-4), 137.54 (C-6), 131.12 (d, J_{CF}=8.4 Hz, C-2″), 128.15 (d, J_{CF}=3.8, C-1″), 127.66 (C-5), 115.43 (d, J_{CF}=21.4 Hz, C-3″), 59.50 (OCH_3), 39.45 (NCH_3); LRMS (ESI): 235, 220, 219 (100%), 162, 135, 120; HRMS (ESI) for $C_{12}H_{12}FN_2O_2$ $[M+H]^+$: calcd 235.0882, found 235.0887; $C_{12}H_{11}FN_2O_2$: calcd C 61.53, H 4.73, N 11.96, found C 61.50, H 4.93, N 11.73.

1.3.4. 4-Methoxy-2-methyl-5-(3-trifluoromethylphenyl)-3(2*H*)-pyridazinone (14). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (97:3); mp 89°C (white solid); ν_{max}: 3075, 3014, 2953, 2858, 1635, 1597, 1450, 1326, 1160, 1116, 809, 702, 512 cm^{-1}; δ_H: 8.00 (s, 1H, H-6), 7.88 (br s, 1H, H-2″), 7.86 (br d, J=7.8 Hz, 1H, H-6″), 7.80 (br d, J=7.8 Hz, 1H, H-4″), 7.72 (t, J=7.8 Hz, 1H, H-5″), 4.02 (s, 3H, OCH_3), 3.70 (s, 3H, NCH_3); δ_C: 157.28 (C-3), 150.66 (C-4), 137.32 (C-6), 132.95 (br, C-6″), 132.91 (C-1″), 129.59 (C-5″), 129.25 (q, J_{CF}=31.8 Hz, C-3″), 127.05 (C-5), 125.40 (br, C-2″ and C-4″), 123.93 (q, J_{CF}=272.6 Hz, CF_3), 59.68 (OCH_3), 39.71 (NCH_3); LRMS (ESI): 285, 270, 269 (100%), 214, 212; HRMS (ESI) for $C_{13}H_{12}F_3N_2O_2$ $[M+H]^+$: calcd 285.0850, found 285.0893; $C_{13}H_{11}F_3N_2O_2$: calcd C 54.93, H 3.90, N 9.86, found C 54.66, H 4.01, N 9.93.

1.3.5. 4-Methoxy-2-methyl-5-(3-thienyl)-3(2*H*)-pyridazinone (15). Yield: 85%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (94:6); mp 72°C (yellow solid); ν_{max}: 3094, 2942, 2854, 1629, 1593, 1311, 1245, 1049, 980, 858, 803, 606, 503 cm^{-1}; δ_H: 8.23 (s, 1H, H-6), 8.17 (dd, J=3 Hz, J=1.3 Hz, 1H, H-2″), 7.70 (dd, J=5.1 Hz, J=3 Hz, 1H, H-5″), 7.64 (dd, J=5.1 Hz J=1.3 Hz, 1H, H-4″), 4.08 (s, 3H, OCH_3), 3.76 (s, 3H, NCH_3); δ_C: 157.46 (C-3), 149.15 (C-4), 136.85 (C-6), 131.85 (C-3″), 127.51 (C-4″), 127.20 (C-2″), 126.52 (C-5″), 123.16 (C-5), 59.15 (OCH_3), 39.33 (NCH_3); LRMS (ESI): 223, 208 (100%), 151, 108; HRMS (ESI) for $C_{10}H_{11}N_2O_2S$ $[M+H]^+$: calcd 223.0541, found 223.0529; $C_{10}H_{10}N_2O_2S$: calcd C 54.04, H 4.53, N 12.60, found C 54.00, H 4.67, N 12.69.

1.3.6. 4-Methoxy-2,5-diphenyl-3(2*H*)-pyridazinone (16). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (98:2); mp 124°C (white solid); ν_{max}: 2941, 1650, 1590, 1493, 1307, 991, 770, 694 cm^{-1}; δ_H: 8.12 (s, 1H, H-6), 7.63 (br d, J=7 Hz, 2H, H-2″), 7.60 (br d, J=7 Hz, 2H, H-2‴), 7.52 (br t, J=7 Hz, 4H, H-3″ and H-3‴), 7.47 (br t, J=7 Hz, 1H, H-4″), 7.43 (br t, J=7 Hz, 1H, H-4‴), 4.01 (s, 3H, OCH_3); δ_C: 157.23 (C-3), 151.25 (C-4), 141.35 (C-1‴), 138.81 (C-6), 131.71 (C-1″), 128.99 (C-4″), 128.88 (C-2″), 128.57 (C-3″), 128.57 (C-3‴), 128.37 (C-5), 128.03 (C-4‴), 125.65 (C-2‴), 59.77 (OCH_3); LRMS (ESI): 279, 263, 236, 201 (100%), 144, 119; HRMS (ESI) for $C_{17}H_{15}N_2O_2$ $[M+H]^+$: calcd 279.1133, found 279.1064; $C_{17}H_{14}N_2O_2$: calcd C 73.37, H 5.07, N 10.07, found C 73.51, H 5.24, N 9.87.

1.3.7. 4-Methoxy-5-(4-methoxyphenyl)-2-phenyl-3(2*H*)-pyridazinone (17). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (98:2); mp 137°C (white

solid); ν_{max}: 3085, 2993, 2962, 2932, 2837, 1644, 1607, 1513, 1305, 1256, 1189, 991, 831, 769, 695, 527 cm^{-1}; δ_H: 8.13 (s, 1H, H-6), 7.63 (d, J=8.8 Hz, 2H, H-2″), 7.59 (br d, J=7.5 Hz, 2H, H-2‴), 7.51 (br t, J=7.5 Hz, 2H, H-3‴), 7.43 (br t, J=7.5 Hz, 1H, H-4‴), 7.07 (d, J=8.8 Hz, 2H, H-3″), 3.99 (s, 3H, 4-OCH_3), 3.82 (s, 3H, 4″-OCH_3); δ_C: 159.85 (C-4″), 157.25 (C-3), 150.62 (C-4), 141.36 (C-1‴), 138.79 (C-6), 130.38 (C-2″), 128.54 (C-3‴), 128.15 (C-5), 127.95 (C-4‴), 125.61 (C-2‴), 123.65 (C-1″), 114.08 (C-3″), 59.55 (4-OCH_3), 55.23 (4″-OCH_3); LRMS (ESI): 309, 294 (100%), 293, 174; HRMS (ESI-MS) for $C_{18}H_{17}N_2O_3$ $[M+H]^+$: calcd 309.1239, found 309.1227; $C_{18}H_{16}N_2O_3$: calcd C 70.12, H 5.23, N 9.09, found C 69.99, H 5.44, N 9.01.

1.3.8. 4-Methoxy-2-phenyl-5-(3-thienyl)-3(2*H*)-pyridazinone (18). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2; mp 116°C (white solid); ν_{max}: 3136, 2955, 1633, 1597, 1400, 1254, 1169, 956, 812, 691 cm^{-1}; δ_H: 8.40 (s, 1H, H-6), 8.17 (br d, J=2.9 Hz, 1H, H-2″), 7.70 (br d, J=4.9 Hz, 1H, H-4″), 7.53 (dd, J=4.9 Hz, J=2.9 Hz, 1H, H-5″), 7.51 (br s, 2H, H-2‴), 7.50 (br t, J=8 Hz, 2H, H-3‴), 7.42 (br t, J=8 Hz, 1H, H-4‴), 4.08 (s, 3H, OCH_3); δ_C: 159.51 (C-3), 154.15 (C-4), 141.98 (C-1‴), 130.14 (C-3″), 129.42 (C-6 and C-4″), 128.52 (C-3‴), 128.11 (C-2″), 127.87 (C-4‴), 125.97 (C-2‴), 123.68 (C-5″), 114.96 (C-5), 57.62 (OCH_3); LRMS (ESI): 285, 151 (100%), 92; HRMS (ESI) for $C_{15}H_{13}N_2O_2S$ $[M+H]^+$: calcd 285.0697, found 285.0722; $C_{15}H_{12}N_2O_2S$: calcd C 63.36, H 4.25, N 9.85, found C 63.25, H 4.02, N 9.90.

1.3.9. 5-Methoxy-2-methyl-4-phenyl-3(2*H*)-pyridazinone (21). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (95:5); mp 128°C (white solid); ν_{max}: 3086, 3055, 3007, 2949, 2852, 1630, 1591, 1460, 1339, 1265, 1164, 968, 864, 780, 698, 492 cm^{-1}; δ_H: 8.22 (s, 1H, H-6), 7.30–7.43 (m, 5H, Ph), 3.90 (s, 3H, OCH_3), 3.67 (s, 3H, NCH_3); δ_C: 160.02 (C-3), 154.87 (C-5), 130.69 (C-1′), 130.16 (C-2′), 128.27 (C-6), 127.67 (C-4′), 127.39 (C-3′), 119.40 (C-4), 57.30 (OCH_3), 39.80 (NCH_3); LRMS (ESI): 217, 201 (100%), 131, 128, 118; HRMS (ESI) for $C_{12}H_{13}N_2O_2$ $[M+H]^+$: calcd 217.0976, found 217.0969; $C_{12}H_{12}N_2O_2$: calcd C 66.65, H 5.59, N 12.96, found C 66.66, H 5.65, N 13.08.

1.3.10. 5-Methoxy-4-(4-methoxyphenyl)-2-methyl-3(2*H*)-pyridazinone (22). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (97:3); mp 105°C (white-yellow solid); ν_{max}: 2963, 2840, 1624, 1468, 1264, 1166, 1105, 1029, 828, 803, 569 cm^{-1}; δ_H: 8.19 (s, 1H, H-6), 7.41 (d, J=9.0 Hz, 2H, H-2′), 6.94 (d, J=9.0 Hz, 2H, H-3′), 3.90 (s, 3H, 5-OCH_3), 3.78 (s, 3H, 4′-OCH_3), 3.67 (s, 3H, NCH_3); δ_C: 160.17 (C-3), 158.74 (C-4′), 154.54 (C-5), 131.56 (C-2′), 128.27 (C-6), 122.58 (C-1′), 119.14 (C-4), 112.86 (C-3′), 57.25 (5-OCH_3), 54.99 (4′-OCH_3), 39.82 (NCH_3); LRMS (ESI): 247, 231, 215, 203, 201 (100%) 161, 148; HRMS (ESI) for $C_{13}H_{15}N_2O_3$ $[M+H]^+$: calcd 247.1082, found 247.1077; $C_{13}H_{14}N_2O_3$: calcd C 63.40, H 5.73, N 11.38, found C 63.64, H 5.48, N 11.47.

1.3.11. 5-Methoxy-2-methyl-4-(4-methylthiophenyl)-3(2*H*)-pyridazinone (23). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (95:5); mp 111°C (white solid); ν_{max}: 3086, 3031, 3001, 2950, 2917, 2851, 1627, 1592, 1487, 1337, 1266, 1165, 970, 866, 822, 501 cm^{-1}; δ_H: 8.20 (s, 1H, H-6), 7.38 (d, J=8.4 Hz, 2H, H-2′), 7.26 (d, J=8.4 Hz, 2H, H-3′), 3.90 (s, 3H, OCH_3), 3.66 (s, 3H, NCH_3), 2.49 (s, 3H, SCH_3); δ_C: 160.02 (C-3), 154.81 (C-5), 137.94 (C-4′), 130.74 (C-2′), 128.26 (C-6), 127.01 (C-1′), 124.75 (C-3′), 118.79 (C-4), 57.35 (OCH_3), 39.89 (NCH_3), 14.48 (SCH_3); LRMS (ESI): 263, 248, 217, 215 (100%), 177; HRMS (ESI) for $C_{13}H_{15}N_2O_2S$ $[M+H]^+$: calcd 263.0854, found 263.0894; $C_{13}H_{14}N_2O_2S$: calcd C 59.52, H 5.38, N 10.68, found C 59.68, H 5.60, N 10.46.

1.3.12. 4-(4-Fluorophenyl)-5-methoxy-2-methyl-3(2*H*)-pyridazinone (24). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (94:6); mp 150°C (white solid); ν_{max}: 3014, 2987, 2951, 2853, 1629, 1597, 1501, 1334, 1222, 1166, 969, 840, 544 cm^{-1}; δ_H: 8.22 (s, 1H, H-6), 7.46 (dd, J_{HH}=9.0 Hz, J_{HF}=5.7 Hz, 2H, H-2′), 7.20 (d, J_{HH}=J_{HF}=9.0 Hz, 2H, H-3′), 3.91 (s, 3H, OCH_3), 3.66 (s, 3H, NCH_3); δ_C: 161.48 (d, J_{CF}=245.1 Hz, C-4′), 159.99 (C-3), 154.93 (C-5), 132.42 (d, J_{CF}=8.1 Hz, C-2′), 128.27 (C-6), 126.86 (d, J_{CF}=3.6 Hz, C-1′), 118.28 (C-4), 114.38 (d, J_{CF}=21.4 Hz, C-3′), 57.38 (OCH_3), 39.87 (NCH_3); LRMS (ESI): 235 (100%), 219, 173, 163, 149, 146, 136; HRMS (ESI) for $C_{12}H_{12}FN_2O_2$ $[M+H]^+$: calcd 235.0882, found 235.0907; $C_{12}H_{11}FN_2O_2$: calcd C 61.53, H 4.73, N 11.96, found C 61.82, H 4.92, N 11.67.

1.3.13. 5-Methoxy-2-methyl-4-(3-trifluoromethylphenyl)-3(2*H*)-pyridazinone (25). Yield: 97%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (99:1); mp 141°C (white solid); ν_{max}: 3125, 3094, 3003, 2958, 2855, 1629, 1589, 1440, 1345, 1261, 1164, 1115, 963, 701, 475 cm^{-1}; δ_H: 8.26 (s, 1H, H-6), 7.77 (br s, 1H, H-2′), 7.73 (br d, J=7.7 Hz, 1H, H-6′), 7.68 (br d, J=7.7 Hz, 1H, H-4′), 7.62 (t, J=7.7 Hz, 1H, H-5′), 3.93 (s, 3H, OCH_3), 3.68 (s, 3H, NCH_3); δ_C: 159.77 (C-3), 155.27 (C-5), 134.38 (C-6′), 131.80 (C-1′), 129.38 (C-5′), 129.17 (q, J_{CF}=31.5 Hz, C-3′), 129.05 (C-6), 127.53 (q, J_{CF}=3.8 Hz, C-2′), 125.19 (q, J_{CF}=3.8 Hz, C-4′), 124.93 (q, J_{CF}=272.5 Hz, CF_3), 117.48 (C-4), 57.52 (OCH_3), 39.88 (NCH_3); LRMS (ESI): 285, 265 (100%), 245; HRMS (ESI) for $C_{13}H_{12}F_3N_2O_2$ $[M+H]^+$: calcd 285.0850, found: 285.0887; $C_{13}H_{11}F_3N_2O_2$: calcd C 54.93, H 3.90, N 9.86, found C 54.86, H 4.02, N 9.99.

1.3.14. 5-Methoxy-4-(3-methoxyphenyl)-2-methyl-3(2*H*)-pyridazinone (26). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (95:5); mp 77°C (white solid); ν_{max}: 2956, 1628, 1597, 1461, 1286, 1162, 1040, 963, 782, 698, 476 cm^{-1}; δ_H: 8.20 (s, 1H, H-6), 7.29 (t, J=8.0 Hz, 1H, H-5′), 6.96 (d, J=8.0 Hz, 1H, H-6′), 6.95 (br s, 1H, H-2′), 6.90 (br d, J=8.0 Hz, 1H, H-4′), 3.89 (s, 3H, 5-OCH_3), 3.73 (s, 3H, 3′-OCH_3), 3.66 (s, 3H, NCH_3); δ_C: 159.98 (C-3), 158.51 (C-3′), 155.01 (C-5), 131.98 (C-1′), 128.49 (C-5′), 128.28 (C-6), 122.54 (C-6′), 119.33 (C-4), 115.98 (C-2′), 113.19 (C-4′), 57.33 (5-OCH_3), 54.97 (3′-OCH_3), 39.86 (NCH_3); LRMS (ESI): 247, 231, 215, 203, 201 (100%), 161, 148; HRMS (ESI) for $C_{13}H_{15}N_2O_3$ $[M+H]^+$: calcd 247.1082, found: 247.1092; $C_{13}H_{14}N_2O_3$: calcd C 63.40, H 5.73, N 11.38, found C 63.33, H 5.59, N 11.45.

1.3.15. 5-Methoxy-2-methyl-4-(2-methylphenyl)-3(2*H*)-pyridazinone (27). Yield: 100%; eluent for flash column

chromatography: CH_2Cl_2–EtOAc (9:1); mp 127°C (white solid); ν_{max}: 3121, 3064, 3022, 2991, 2949, 2857, 1628, 1591, 1463, 1333, 1262, 1185, 960, 872, 744, 604, 472 cm^{-1}; δ_H: 8.20 (s, 1H, H-6), 7.24 (m, 2H, H-3′ and H-4′), 7.18 (m, 1H, H-5′), 7.05 (br d, J=7.4 Hz, 1H, H-6′), 3.84 (s, 3H, 5-OCH_3), 3.67 (s, 3H, NCH_3), 2.04 (s, 3H, 2′-CH_3); δ_C: 160.08 (C-3), 155.56 (C-5), 136.74 (C-2′), 131.00 (C-1′), 130.15 (C-6′), 129.61 (C-3′), 128.13 (C-6), 127.92 (C-4′), 125.26 (C-5′), 120.22 (C-4), 57.26 (OCH_3), 39.81 (NCH_3), 19.22 (2′-CH_3); LRMS (ESI): 231 (100%), 215, 199, 145, 142, 132; HRMS (ESI) for $C_{13}H_{15}N_2O_2$ $[M+H]^+$: calcd 231.1133, found: 231.1159; $C_{13}H_{14}N_2O_2$: calcd C 67.81, H 6.13, N 12.17, found C 67.69, H 6.27, N 11.56.

1.3.16. 4-(2,4-Dichlorophenyl)-5-methoxy-2-methyl-3(2*H*)-pyridazinone (28). Yield: 90%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (98:2); mp 131°C (white solid); ν_{max}: 3086, 3053, 2955, 1622, 1597, 1462, 1340, 1276, 1169, 964, 875, 488 cm^{-1}; δ_H: 8.26 (s, 1H, H-6), 7.67 (d, J=2.1 Hz, 1H, H-3′), 7.46 (dd, J=8.3 Hz, J=2.1 Hz, 1H, H-5′), 7.30 (d, J=8.3 Hz, 1H, H-6′), 3.90 (s, 3H, OCH_3), 3.67 (s, 3H, NCH_3); δ_C: 159.26 (C-3), 155.95 (C-5), 134.29 (C-2′), 133.53 (C-4′), 133.38 (C-6′), 129.55 (C-1′), 128.61 (C-3′), 127.92 (C-6), 127.07 (C-5′), 116.81 (C-4), 57.46 (OCH_3), 39.67 (NCH_3); LRMS (ESI): 285/287/289, product ions from 285: 249 (100%), 235, 207, 186; HRMS (ESI) for $C_{12}H_{11}Cl_2N_2O_2$ $[M+H]^+$: calcd 285.0197, found 285.0199; $C_{12}H_{10}Cl_2N_2O_2$: calcd C 50.55, H 3.54, N 9.82, found C 50.48, H 3.60, N 9.77.

1.3.17. 5-Methoxy-2,4-diphenyl-3(2*H*)-pyridazinone (29). Yield: 100%; eluent for flash column chromatography: CH_2Cl_2–EtOAc (98:2); mp 127°C (white solid); ν_{max}: 3057, 2944, 2857, 1641, 1592, 1490, 1262, 955, 765, 694, 567 cm^{-1}; δ_H: 8.13 (s, 1H, H-6), 7.65 (br d, J=7 Hz, 2H, H-2′), 7.61 (br d, J=7 Hz, 2H, H-2‴), 7.53 (br t, J=7 Hz, 4H, H-3′ and H-3‴), 7.48 (br t, J=7 Hz, 1H, H-4′), 7.45 (br t, J=7 Hz, 1H, H-4‴), 4.03 (s, 3H, OCH_3); δ_C: 157.22 (C-3), 151.24 (C-5), 141.34 (C-1‴), 138.81 (C-6), 131.70 (C-1′), 128.98 (C-4′), 128.87 (C-2′), 128.56 (C-3′ and C-3‴), 128.36 (C-4), 128.01 (C-4‴), 125.63 (C-2‴), 59.76 (OCH_3); LRMS (ESI): 279, 263 (100%), 236, 144, 119; HRMS (ESI) for $C_{17}H_{15}N_2O_2$ $[M+H]^+$: calcd 279.1133, found 279.1179; $C_{17}H_{14}N_2O_2$: calcd C 73.37, H 5.07, N 10.07, found C 73.38, H 5.15, N 10.10.

1.3.18. 5-Methoxy-4-(4-methoxyphenyl)-2-phenyl-3(2*H*)-pyridazinone (30). Yield: 94%; eluent for flash column chromatography: heptane–EtOAc (2:1); mp 146°C (white solid); ν_{max}: 3066, 3024, 2951, 2846, 1634, 1609, 1447, 1297, 1257, 1182, 1036, 843, 760, 692, 557 cm^{-1}; δ_H: 8.39 (s, 1H, H-6), 7.33–7.56 (m, 5H, Ph), 7.44 (d, J=8.9 Hz, 2H, H-2′), 6.96 (d, J=8.9 Hz, 2H, H-3′), 3.97 (s, 3H, 5-OCH_3), 3.78 (s, 3H, 4′-OCH_3); δ_C: 159.97 (C-3), 158.88 (C-4′), 154.37 (C-5), 141.93 (C-1‴), 131.71 (C-2′), 129.78 (C-6), 128.49 (C-3‴), 127.77 (C-4‴), 125.84 (C-2‴), 122.48 (C-1′), 120.02 (C-4), 112.94 (C-3′), 57.48 (5-OCH_3), 55.04 (4′-OCH_3); LRMS (ESI): 309, 175 (100%); HRMS (ESI) for $C_{18}H_{17}N_2O_3$ $[M+H]^+$: calcd 309.1239, found 309.1203; $C_{18}H_{16}N_2O_3$: calcd C 70.12, H 5.23, N 9.09, found C 69.88, H 5.40, N 8.84.

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