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Palladium-Catalysed Multicomponent Aminocarbonylation of Aryl or Heteroaryl Halides with [Mo(CO)$_6$] and Aryl- or Heteroarylamines Using Conventional Heating

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Di(hetero)arylamides have been synthesized in short reaction times by palladium-catalysed multicomponent aminocarbonylation of either electron-deficient or electron-rich heteroaryl halides and *p*-iodoanisole with several arylamines bearing either electron-donating or -withdrawing groups and aminopyridines using [Mo(CO)$_6$] as a solid CO source and conventional heating. Starting from heteroaryl bromides, a palladacycle with tBu$_3$PHBF$_4$ as ligand is required together with DBU as a base in dioxane and a temperature of 125 °C. From (hetero)aryl iodides, Pd(OAc)$_2$ without a ligand and DBU were used in dioxane at 110 °C. Under the latter conditions we were able to apply this reaction to deactivated aminopyridines to obtain the corresponding di(hetero)arylamides. We have demonstrated that these reactions can be performed under conventional heating (110–125 °C) to yield the corresponding di(hetero)arylamides in moderate-to-high yields in short reaction times (from 1–3 h) with no need for MW irradiation. A *N*-substituted isoindoline-1,3-dione from 2-iodobenzoic acid or methyl 2-iodobenzoate and *p*-anisidine through a one-step carbonylative cyclization reaction was also obtained. Thus, we have extended the scope of this palladium-catalysed aminocarbonylation reaction with [Mo(CO)$_6$] to several (hetero)aryl substrates using conventional heating.

Introduction

Palladium-catalysed carbonylation of aryl halides is a highly efficient method for the synthesis of carbonyl compounds.[1,2] Particularly important is the aminocarbonylation reaction, which is a selective and useful method for the direct synthesis of amides through the coupling of halides with primary/secondary amines. However, in comparison with other transition-metal-mediated reactions, such as cross-couplings and Heck and Sonogashira reactions, transition-metal-mediated carbonylation and aminocarbonylation reactions for the functionalization of aryl or heteroaryl halides have seldom been explored.

Most of the aminocarbonylation reactions that have been reported use carbon monoxide gas as the CO source.[2–4] The scope of this reaction is broad and the tolerance for different functional groups is high. However, although this type of reaction has been extensively used in large-scale production, its true potential has not been fully exploited in laboratory-scale syntheses. In particular, the cumbersome handling of CO gas and the long reactions times (ranging from hours to days) severely limit the usefulness of this carbonylative transformation in drug discovery and other small-scale applications.

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Other operational advances in the conversion of aryl halides into diarylamides have included the use of solid [Mo(CO)$_6$] as the carbon monoxide source and microwave reactors to facilitate these transformations.[5–7] Wannberg and Larhed[6] improved the CO release from a tandem [Mo(CO)$_6$]/amidation methodology by using DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) as a base and THF as solvent in microwave protocols. With this more general method they were able to accomplish aminocarbonylations using aniline, benzylamine, the sterically hindered *tert*-butylamine and amino acids. The same authors performed two experiments starting with aryl iodides, [Mo(CO)$_6$] and amines using conventional heating with no significant change in the product yield but the general procedure reported was performed under MW irradiation. This reaction has already been described with heteroaryl halides such as bromopyridines, bromopyrimidines and bromoquinolines among others reacting with alkylamines.[7] However, electron-rich heterocycles, like halothiophenes, have been less used.

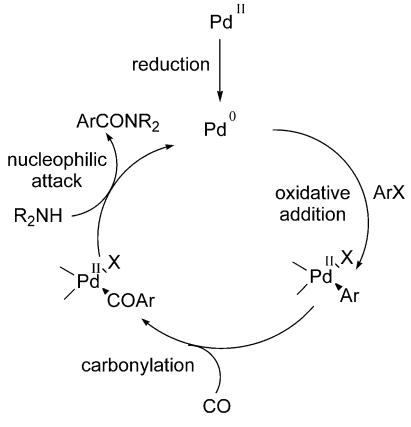
Some carbonylation reactions using [Mo(CO)$_6$] have also been described without the assistance of microwave heating. Yamazaki and Kondo performed a solid-phase palladium-catalysed aminocarbonylation of aryl halides using CO generated in situ from [Mo(CO)$_6$] by ligand exchange with CH$_3$CN at 80 °C. They used Pd(OAc)$_2$ as the catalyst, BINAP [2,2′-bis(diphenylphosphanyl)-1,1′-binaphthyl] as the ligand and Cs$_2$CO$_3$ as the base.[8] The same research group has described a palladium-catalysed double carbonylation

of aryl iodides with alkylamines using tBu$_3$P as the ligand, [Mo(CO)$_6$] and DBU at room temperature.[9] They also used tBu$_3$P in the palladium-catalysed [Pd(tBu$_3$P)$_2$]-alkynylcarbonylation of aryl iodides with phenylacetylene and [Mo(CO)$_6$] in the presence of CH_3CN and Et_3N at room temperature.[10]

Herein we report the use of [Mo(CO)$_6$] in the multicomponent palladium-assisted aminocarbonylation of electron-deficient and -rich heteroaryl halides and iodoanisole with several (hetero)arylamines to give the corresponding di-(hetero)arylamides using conventional heating for 1–3 h, thus extending the scope of this reaction. Palladium acetate was used as the palladium source with the (hetero)aryl iodides and *trans*-di-μ-acetatobis[2-(di-*o*-tolylphosphanyl)-benzyl]dipalladium(II), also known as "Herrmann's palladacycle",[11,12] was used with the (hetero)aryl bromides. With the latter, tBu$_3$PHBF$_4$ was used as the ligand and, in both cases, DBU was used as the base.[6,7]

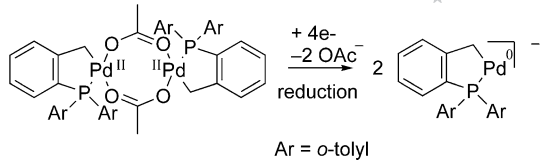
Results and Discussion

The general mechanism for the aminocarbonylation reaction using gaseous carbon monoxide is illustrated in Scheme 1.[13] The active catalytic species is a Pd^0 complex. The oxidative addition of the aryl halide to the metal centre is followed by the insertion of CO into the intermediate aryl complex. In contrast to coupling reactions, the final step in the aminocarbonylation is the nucleophilic attack of the amine on the acylpalladium complex rather than reductive elimination.



Scheme 1. General catalytical cycle for the aminocarbonylation of aryl halides.

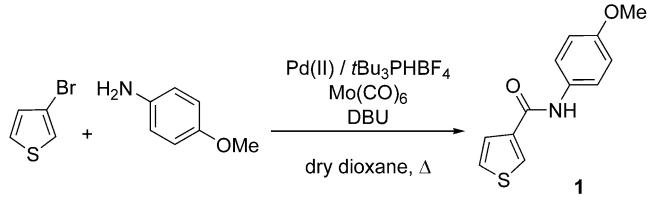
With (hetero)aryl bromides, a palladacycle, Herrmann's catalyst {*trans*-di-μ-acetatobis[2-(di-*o*-tolylphosphanyl)benzyl]dipalladium(II)}, was used as the catalyst, the active catalytic species being the Pd^0 ionic complex resulting from the reduction of the initial Pd^{II} complex without rupture of the carbon–palladium bond (Scheme 2).[11,12]



Scheme 2. Formation of the active Pd^0 ionic complex from Herrmann's palladacycle.

As bromo derivatives are more easily available than their iodo counterparts, they were initially used in these aminocarbonylation reactions. On the basis of the catalytic cycle, the presence of electron-donating groups in the amines should favour attack on the acylpalladium complex as they increase the electron density on the amine group, thus enhancing its nucleophilicity. Thus, we first studied the reactivity of 3-bromothiophene with the activated *p*-anisidine to determine the most effective conditions (Table 1).

Table 1. Aminocarbonylation of 3-bromothiophene.[a]



Entry	Hermann's catalyst [mol-%]	tBu$_3$PHBF$_4$ [mol-%]	Temp. [°C]	Time [h]	% Yield
1	4	8	110	6	10
2	4	8	125	1	72
3	2.4	5	125	1	68

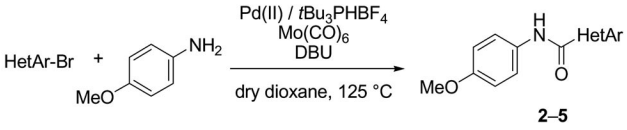
[a] Reagents and conditions: *p*-anisidine (1.4 equiv.), Herrmann's palladacycle (2.4–4.0 mol-%), tBu$_3$PHBF$_4$ (5.0–8.0 mol-%), DBU (0.7 equiv.) and [Mo(CO)$_6$] (0.5 equiv.).

Analysis of Table 1 shows that whereas decreasing the amounts of the catalytic components from 4 mol-% of Pd catalyst and 8 mol-% of ligand (entry 2) to 2.4 mol-% of Pd catalyst and 5 mol-% of ligand (entry 3) did not seem to influence significantly the yield, the reaction temperature is of great importance, as heating at 110 °C provided the carboxamide **1** in only 10% yield on heating for 6 h (entry 1). By heating at 125 °C, compound **1** was obtained in high yields (entries 2 and 3) in only 1 h.

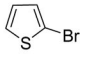
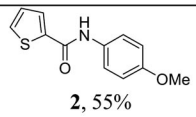
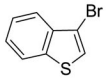
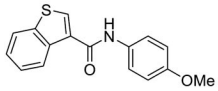
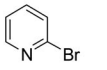
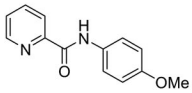
More experiments were performed with *p*-anisidine and several electron-rich and -deficient heteroaryl bromides using the conditions of entry 2 or 3 of Table 1. The results are presented in Table 2.

In all cases presented in Table 2, the use of the highest amounts of the catalytic components provided the best yields, and in the reaction involving 3-bromothiophene the reaction time was also significantly reduced (Table 2, compound **2**). Concerning the reaction with 2-bromopyridine, the use of higher amounts of the catalytic components was also required to obtain the best yield, but in this case, 2-bromopyridine had to be used in excess as well (Table 2).

Table 2. Carbonylation of *p*-anisidine with several heteroaryl bromides.



2–5

Bromo derivative	Catalytic system	Time	Yield
	2.4 mol-% catalyst 5 mol-% tBu_3PHBF_4	3.5 h	 **2**, 55%
	4 mol-% catalyst 8 mol-% tBu_3PHBF_4	1 h	**2**, 66%
	2.4 mol-% catalyst 5 mol-% tBu_3PHBF_4	1 h	 **3**, 40%
	4 mol-% catalyst 8 mol-% tBu_3PHBF_4	1 h	**3**, 60%
	2.4 mol-% catalyst 5 mol-% tBu_3PHBF_4	1 h	 **4**, 30%
	4 mol-% catalyst 8 mol-% tBu_3PHBF_4	1 h	**4**, 40%
	4 mol-% catalyst 8 mol-% tBu_3PHBF_4	1 h	**4**, 60%[a]

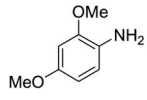
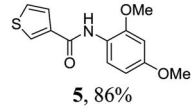
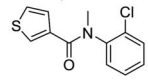
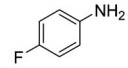
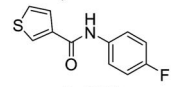
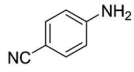
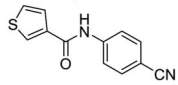
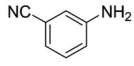
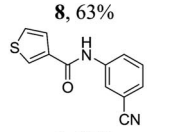
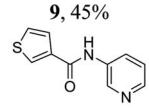
[a] 1.4 equiv. of 2-bromopyridine and 1.0 equiv. of *p*-anisidine.

As the best result was obtained with 3-bromothiophene (Table 1, entry 2; compound **1** was obtained in 72% yield), it was decided to study its reactivity in aminocarbonylation reactions with various arylamines bearing either electron-donating (EDG) or -withdrawing (EWG) groups (Table 3). The reaction involving 2,4-dimethoxyaniline gave product **5** in an excellent yield (86%), which shows that the presence of two EDGs in the *ortho* and *para* positions is important. The reaction with 2-chloro-*N*-methylaniline, a secondary arylamine, gave compound **6** in only 30% yield. This moderate yield could be due to the presence of an EWG in the *ortho* position.

Reactions with anilines bearing EWGs also successfully afforded the expected (hetero)arylamides. Thus, compound **7**, which results from the reaction with 4-fluoroaniline, was obtained in high yield (70%) and reactions with deactivated amines bearing a nitrile group, 4- and 3-aminobenzonitrile, also afforded the expected amides **8** and **9** in moderate-to-good yields. In the latter case, the presence of the cyano group in the *meta* position led to a decrease in the yield of the corresponding product. With deactivated aminopyridines the results were more disappointing: reaction with 3-aminopyridine gave heteroarylamide **10** in only 15% yield, whereas no reaction occurred using 2-aminopyridine on heating for 6 h (Table 3) and the starting materials were recovered.

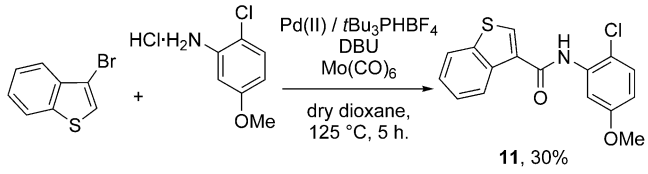
The aminocarbonylation reaction was also performed on 3-bromobenzo[*b*]thiophene with 2-chloro-5-methoxyaniline

Table 3. Aminoarbonylation of 3-bromothiophene with various arylamines.[a]

Bromo derivative	Amine	Time	Yield
		1 h	 **5**, 86%
		1 h	 **6**, 30%[b]
		1 h	 **7**, 70%
		1 h	 **8**, 63%
		1 h	 **9**, 45%
		3 h	 **10**, 15%
		6 h	/

[a] Reagents and conditions: 3-bromothiophene (1.0 equiv.), arylamine (1.4 equiv.), Pd^{II} (4.0 mol-%), tBu_3PHBF_4 (8.0 mol-%), DBU (0.7 equiv.) and $[Mo(CO)_6]$ (0.5 equiv.) at 125 °C in dry dioxane. [b] 2-chloro-*N*-methylaniline (1.0 equiv.) and 3-bromothiophene (1.4 equiv.).

hydrochloride; (hetero)arylamide **11** was obtained in only 30% yield on heating for 5 h (Scheme 3), which confirms the effect of an *o*-chlorine atom in the aniline already observed for amide **6** (Table 2).



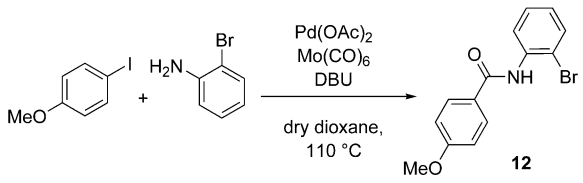
11, 30%

Scheme 3. Reaction of 3-bromobenzo[*b*]thiophene and 2-chloro-5-methoxyaniline hydrochloride.

With these results in hand, we then studied the reactivity of some iodo derivatives in these aminocarbonylation reactions to see if better results could be obtained. The catalytic system was changed: phosphane- or ligand-free Pd catalysts are active in the coupling of aryl iodides (but not of aryl bromides).[12] Thus, "Herrmann's palladacycle" was re-

placed by $Pd(OAc)_2$ and no ligand was used. Several reaction conditions were tested using 4-iodoanisole and 2-bromoaniline (Table 4).

Table 4. Aminocarbonylation of 4-iodoanisole with 2-bromoaniline.[a]

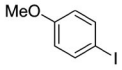
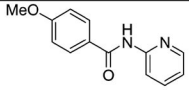
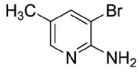
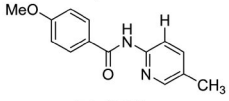
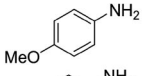
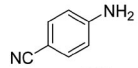
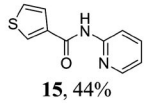


	2-Bromoaniline (equiv.)	DBU (equiv.)	$[Mo(CO)_6]$ (equiv.)	Time [h]	% Yield
1	1.4	1.5	0.5	1	54
2	2.5	3.0	1.0	1	72

[a] Reagents and conditions: $Pd(OAc)_2$ (10 mol-%), DBU and $[Mo(CO)_6]$ at 110 °C in dry dioxane.

The conditions used in entry 2 (Table 4) gave the best yield of the amide **12**. Performing the reaction at 125 °C did not lead to an increase in the yield. Thus, it was decided to use these conditions with other aryl and heteroaryl iodides in the aminocarbonylation reactions with (hetero)arylamines at 110 °C (Table 5).

Table 5. Aminocarbonylation of aryl and heteroaryl iodides with aryl or heteroarylamines.

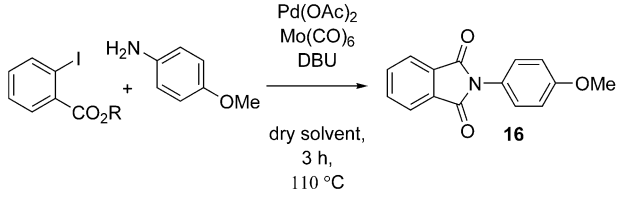
Iodo derivative	Amine	Time	Yield
		1 h	 **13**, 76%
		3 h	 **14**, 25%
		1 h	**2**, 65%
		1 h	**8**, 70%
		3 h	**10**, 55%
		3 h	 **15**, 44%

Reactions with 4-iodoanisole and 2-aminopyridine gave amide **13** in an unexpectedly high yield (76%), which shows that even deactivated amines can be used under these conditions. However, the use of the more cumbersome 2-amino-3-bromo-5-methylpyridine provided the debrominated amide **14** in a rather poor yield (only 25%).

Reactions with 2- and 3-iodothiophene were also performed with various (hetero)arylamines. Compound **2**, which results from the reaction of 2-halothiophene and *p*-anisidine, was obtained in the same yield (≈65%) using either 2-iodothiophene (Table 5) or 2-bromothiophene (Table 2). With 4-aminobenzonitrile, the yield of amide **8** obtained with 3-iodothiophene (Table 5, 70%) was only slightly higher than that obtained with 3-bromothiophene (Table 3, 63%). Nevertheless, with aminopyridines, a wider range of yields was noted: reaction of 3-iodothiophene with 3-aminopyridine afforded the heteroarylamide **10** in 55% yield, which was obtained in only 15% with 3-bromothiophene (Table 3). The heteroarylamine **15**, which results from the reaction of 3-iodothiophene and 2-aminopyridine, was obtained in good yield (Table 5, 44%), but no reaction occurred with 3-bromothiophene (Table 3). These results show that iodo derivatives are more reactive than the corresponding bromo compounds when deactivated amines are used.

We also performed the aminocarbonylations of 2-iodobenzoic acid and methyl 2-iodobenzoate with *p*-anisidine and obtained the isoindoline-1,3-dione **16** after intramolecular cyclization in a one-pot procedure (Table 6). This reaction has already been described by Worlikar and Larock,[14] who showed that the reactions of *o*-iodobenzoates with primary amines in the presence of gaseous carbon monoxide, $Pd(OAc)_2$ as catalyst and Cs_2CO_3 as base successfully afforded isoindoline-1,3-diones. Unfortunately, in our case, the yields were very poor; compound **16** was synthesized in yields of 10% with the acid in dioxane (Table 6, entry 1) and 35% when the ester was used in toluene (Table 6, entry 3).

Table 6. Aminocarbonylation of 2-iodobenzoic acid and the methyl ester.



Entry	Solvent	R	% Yield
1	dioxane	H	10
2	dioxane	OMe	20
3	toluene	OMe	35

[a] Reagents and conditions: $Pd(OAc)_2$ (10 mol-%), DBU (3.0 equiv.) and $[Mo(CO)_6]$ (1.0 equiv.) at 110 °C in dry solvents.

Conclusions

We have demonstrated that $[Mo(CO)_6]$ can be successfully used as a CO source in aminocarbonylation reactions without requiring microwave irradiation. All the reactions were performed using conventional heating in short reaction times (1–3 h), thus extending the scope of the reaction.

Di(hetero)arylamides resulting from halothiophenes and arylamines bearing either electron-withdrawing or -donating groups were successfully synthesized, with no significant improvement in yields noted when iodothiophenes were used in place of bromothiophenes. However, with deactivated heteroarylamines, iodo derivatives were significantly more reactive than the corresponding bromo compounds. In this work we have also increased the range of (hetero)-aryl substrates, either halides or amines, that can be used in the aminocarbonylation reaction.

Experimental Section

General Methods: Melting points were determined with a Gallenkamp apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Unity Plus spectrometer at 300 and 75.4 MHz, respectively, or with a Bruker Avance II$^+$ spectrometer at 400 and 100.6 MHz, respectively. Two-dimensional ^{1}H–^{1}H and ^{1}H–^{13}C correlations were performed to assign some of the signals. EI-MS and HRMS spectra were recorded by the Mass Spectrometry Service of the University of Vigo, Spain. The ESI mass spectra were recorded with a Thermo Finnigan LXQ LC-MS spectrometer by direct injection using MeOH as solvent. The IR spectra were recorded as Nujol mulls using NaCl cells with a Bomem FTLA-2000-104 spectrometer. Elemental analysis was performed on a LECO CHNS 932 elemental analyser.

The reactions were monitored by thin-layer chromatography (TLC). Column chromatography was performed with Macherey–Nagel silica gel (230–400 mesh). Petroleum ether refers to the boiling range 40–60 °C. When a solvent gradient was used, unless stated otherwise, the polarity was increased from neat petroleum ether to mixtures of diethyl ether/petroleum ether, increasing in steps of 10% diethyl ether until the product was isolated.

Typical Experimental Conditions for the Aminocarbonylation Reactions

Conditions A: The heteroaryl bromide was added to a Schlenk tube containing dry dioxane (1–2 mL per 0.5 mmol of bromide). Then the (hetero)arylamine (1.4 equiv.), DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene; 0.7 equiv.), *trans*-di-μ-acetatobis[2-(di-*o*-tolyphosphanyl)benzyl]dipalladium(II) (4 mol-%), tri-*tert*-butylphoshonium tetrafluoroborate (8 mol-%) and molybdenum hexacarbonyl (0.5 equiv.) were successively added and the solution was heated at 125 °C in a silicone bath for 1–5 h, unless stated otherwise (see Tables 1, 2 and Scheme 3).

Conditions B: The (hetero)aryl iodide was added to a Schlenk tube containing dry dioxane (1–2 mL per 0.5 mmol of iodide). Then the (hetero)arylamine (2.5 equiv.), DBU (3.0 equiv.), palladium acetate(II) (10 mol-%) and molybdenum hexacarbonyl (1.0 equiv.) were successively added and the solution was heated at 110 °C in a silicone bath for 1–3 h (see Tables 4 and 5).

General Work-up: The reactions were monitored by TLC, following the disappearance of the halo derivative. After cooling, dichloromethane was added, the mixture was transferred to a round-bottomed flask and the solvents were removed under reduced pressure. The resulting oils were submitted to column chromatography to give the products as solids.

***N*-(4-Methoxyphenyl)thiophene-3-carboxamide (1):** From 3-bromothiophene (100 mg, 0.610 mmol) and *p*-anisidine (106 mg, 0.860 mmol) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 50% diethyl ether/petroleum ether, compound **1** was obtained as an off-white solid (103 mg, 72%). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 163–165 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 6.89 (d, J = 9.3 Hz, 2 H, 3′-, 5′-H), 7.38 (dd, J = 4.8, 3.0 Hz, 1 H, 5-H), 7.47–7.53 (m, 3 H, 2′-, 6′-, 4-H), 7.76 (br. s, 1 H, NH), 7.96 (br. s, 1 H, 2-H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.47 (OCH_3), 114.19 (2 CH, 3′-, -5′-CH), 122.23 (2 CH, 2′-, 6′-CH), 126.12 (4-CH), 126.72 (5-CH), 128.49 (2-CH), 130.74 (C-1'), 137.79 (C-3), 156.60 (C-4'), 161.17 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3328 (NH), 3111 (NH), 1644 (C=O) cm^{-1}. MS (EI): m/z (%) = 234 (5) [M + 1]$^+$, 233 (35) [M]$^+$, 111 (100) [M – 122]$^+$. HRMS: calcd. for $C_{12}H_{11}NO_2S$ [M]$^+$ 233.0511; found 233.0514.

***N*-(4-Methoxyphenyl)thiophene-2-carboxamide (2):** From 2-bromothiophene (100 mg, 0.610 mmol) and *p*-anisidine (106 mg, 0.860 mmol) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% diethyl ether/petroleum ether, or from 2-iodothiophene (100 mg, 0.480 mmol) and *p*-anisidine (143 mg, 1.19 mmol) using conditions B and after purification by column chromatography using a solvent gradient from neat petroleum ether to 35% diethyl ether/petroleum ether, compound **2** was obtained as an off-white solid (95.0 mg, 66%; 94.0 mg, 65%, respectively). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 143–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 6.89 (d, J = 9.3 Hz, 2 H, 3′-, 5′-H), 7.11 (dd, J = 4.8, 3.6 Hz, 1 H, 4-H), 7.49–7.54 (m, 3 H, 2′-, 6′-, 5-H), 7.62 (dd, J = 3.6, 0.9 Hz, 1 H, 3-H), 7.75 (br. s, 1 H, NH) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.47 (OCH_3), 114.21 (2 CH, 3′-, 5′-CH), 122.22 (2 CH, 2′-, 6′-CH), 127.75 (4-CH), 128.32 (3-CH), 130.48 (5-CH), 130.56 (C-1'), 139.26 (C-2), 156.67 (C-4'), 159.94 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3282 (NH), 3081 (NH), 1627 (C=O) cm^{-1}. $C_{12}H_{11}NO_2S$ (233.29): calcd. C 61.78, H 4.75, N 6.00, S 13.74%; found C 61.73, H 4.80, N 6.01, S 13.95.

***N*-(4-Methoxyphenyl)benzo[*b*]thiophene-3-carboxamide (3):** From 3-bromobenzo[*b*]thiophene (100 mg, 0.470 mmol) and *p*-anisidine (81.0 mg, 0.660 mmol) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 50% diethyl ether/petroleum ether, compound **3** was obtained as an off-white solid (80.0 mg, 60%). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 207–209 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.74 (s, 3 H, OCH_3), 6.93 (d, J = 9.2 Hz, 2 H, 3′-, 5′-H), 7.41–7.49 (m, 2 H), 7.66 (d, J = 9.2 Hz, 2 H, 2'-, 6′-H), 8.05–8.07 (m, 1 H, 7-H), 8.39–8.41 (m, 1 H, 4 H), 8.49 (s, 1 H, 2-H), 10.20 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 55.21 (OCH_3), 113.83 (2 CH, 3'-, 5′-CH), 121.81 (2 CH, 2′-, 6′-CH), 122.85 (7-CH), 124.33 (4-CH), 124.93 (CH), 125.00 (CH), 131.27 (C-3, 2-CH), 132.11 (C-1'), 137.19 (C), 139.43 (C), 155.54 (C-4'), 161.58 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3292 (NH), 3089 (NH), 1641 (C=O) cm^{-1}. MS (EI): m/z (%) = 284 (6) [M + 1]$^+$, 283 (32) [M]$^+$, 161 (100) [M – 122]$^+$. HRMS: calcd. for $C_{16}H_{13}NO_2S$ [M]$^+$ 283.0667; found 283.0663.

***N*-(4-Methoxyphenyl)picolinamide (4):** From 2-bromopyridine (88.0 mg, 0.560 mmol) and *p*-anisidine (49.0 mg, 0.400 mmol) using modified conditions A (Table 2) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% diethyl ether/petroleum ether, compound **4** was obtained as a yellow solid (55.0 mg, 60%). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 96–98 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 6.94 (d, J = 9.2 Hz, 2 H, 3′-, 5′-H), 7.47–7.50 (m, 1 H, 5-H), 7.71 (d, J = 9.2 Hz, 2 H,

2′-, 6′-H), 7.92 (dt, J = 7.6, 1.6 Hz, 1 H, 4-H), 8.31 (br. d, J = 7.6 Hz, 1 H, 3-H), 8.62 (br. d, J = 3.6 Hz, 1 H, 6-H), 9.35 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 55.48 (OCH_3), 114.23 (2 CH, 3′-, 5′-CH), 121.24 (2 CH, 2′-, 6′-CH), 122.38 (3-CH), 126.30 (5-CH), 131.00 (C-1'), 137.73 (CH), 147.80 (6-CH), 149.90 (C-2), 156.39 (C-4'), 161.61 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3355 (NH), 1682 (C=O) cm^{-1}. MS (EI): m/z (%) = 229 (9) [M + 1]$^+$, 228 (100) [M]$^+$, 79 (53) [M – 149]$^+$, 78 (56) [M – 150]$^+$. HRMS: calcd. for $C_{13}H_{12}N_2O_2$ [M]$^+$ 228.0899; found 228.0896.

***N*-(2,4-Dimethoxyphenyl)thiophene-3-carboxamide (5):** From 3-bromothiophene (65.0 mg, 0.400 mmol) and 2,4-dimethoxyaniline (86.0 mg, 0.560 mmol) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% diethyl ether/petroleum ether, compound **5** was obtained as an off-white solid (89.0 mg, 86%). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 151–153 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 3.90 (s, 3 H, OCH_3), 6.51–6.55 (m, 2 H, 3'-, 5′-H), 7.38–7.40 (m, 1 H, 5-H), 7.48–7.50 (m, 1 H, 2-H), 7.96–7.97 (m, 1 H, 4-H), 8.17 (br. s, 1 H, NH), 8.36 (d, J = 9.6 Hz, 1 H, 6′-H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.40 (OCH_3), 55.81 (OCH_3), 98.63 (CH), 103.82 (CH), 120.68 (6′-CH), 121.16 (C-1'), 126.05 (2-CH), 126.63 (5-CH), 128.27 (4-CH), 138.30 (C-3), 149.31 (C-2'), 156.46 (C-4'), 160.54 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3261 (NH), 3091 (NH), 1644 (C=O) cm^{-1}. MS (EI): m/z (%) = 264 (5) [M + 1]$^+$, 263 (54) [M]$^+$, 111 (100) [M – 152]$^+$. HRMS: calcd. for $C_{13}H_{13}NO_3S$ [M]$^+$ 263.0616; found 263.0616.

***N*-(2-Chlorophenyl)-*N*-methylthiophene-3-carboxamide (6):** From 3-bromothiophene (1.40 equiv., 91.0 mg, 0.560 mmol) and 2-chloro-*N*-methylaniline (1.00 equiv., 57.0 mg, 0.400 mmol) using modified conditions A (Table 3) and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% diethyl ether/petroleum ether, compound **6** was obtained as a yellow solid (30.0 mg, 30%). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 165–167 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.38 (s, 3 H, NCH_3), 6.96–6.99 (m, 1 H), 7.03–7.07 (m, 1 H), 7.19–7.29 (m, 4 H), 7.44–7.46 (m, 1 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 37.05 (NCH_3), 124.56 (CH), 128.02 (CH), 128.06 (CH), 128.95 (CH), 129.23 (CH), 130.18 (CH), 130.66 (CH), 132.70 (C), 136.45 (C), 142.10 (C), 162.24 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 1647 (C=O) cm^{-1}. MS (EI): m/z (%) = 253.02 (0.4) [M, ^{37}Cl]$^+$, 251.02 (1) [M, ^{35}Cl]$^+$, 216 (100) [M – Cl]$^+$, 110.97 (100) [M – 140]$^+$. HRMS: calcd. for $C_{12}H_{10}ClNOS$ [M, ^{37}Cl] 253.0142, [M, ^{35}Cl] 251.0172; found 253.0138, 251.0182.

***N*-(4-Fluorophenyl)thiophene-3-carboxamide (7):** From 3-bromothiophene (100 mg, 0.610 mmol) and *p*-fluoroaniline (95.0 mg, 0.860 mmol) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 40% diethyl ether/petroleum ether, compound **7** was obtained as an off-white solid (95.0 mg, 70%). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 165–167 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.03–7.08 (m, 2 H, 3'-, 5′-H), 7.39–7.41 (m, 1 H, 5-H), 7.48–7.50 (m, 1 H, 4-H), 7.55–7.60 (m, 2 H, 2′-, 6′-H), 7.75 (br. s, 1 H, NH), 7.97–7.99 (m, 1 H, 2-H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 115.73 (d, J = 22.4 Hz, 2 CH, 3′-, 5′-CH), 122.15 (d, J = 8.1 Hz, 2 CH, 2′-, 6′-CH), 126.04 (4-CH), 126.96 (5-CH), 128.77 (2-CH), 133.66 (d, J = 3.2 Hz, C-1′), 137.50 (C-3), 159.72 (d, J = 244 Hz, CF), 161.15 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3326 (NH), 1647 (C=O) cm^{-1}. $C_{11}H_8FNOS$ (221.25): C 59.71, H 3.64, N 6.33, S 14.49; found C 59.59, H 3.70, N 6.32, S 14.65.

***N*-(4-Cyanophenyl)thiophene-3-carboxamide (8):** From 3-bromothiophene (163 mg, 1.00 mmol) and 4-aminobenzonitrile (165 mg, 1.40 mmol) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 70% diethyl ether/petroleum ether, or from 3-iodothiophene (100 mg, 0.480 mmol) and 4-aminobenzonitrile (141 mg, 1.19 mmol) using conditions B and after purification by column chromatography using a solvent gradient from neat petroleum ether to 60% diethyl ether/petroleum ether, compound **8** was obtained as a yellow solid (143 mg, 63%; 159 mg, 70%, respectively). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 157–159 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.63 (dd, J = 5.2, 1.2 Hz, 2 H, 4-H), 7.67 (dd, J = 5.2, 2.8 Hz, 1 H, 5-H), 7.80 (d, J = 8.8 Hz, 2 H, 3′-, 5′-H), 7.95 (d, J = 8.8 Hz, 2 H, 2′-, 6′-H), 8.40 (dd, J = 2.8, 1.0 Hz, 1 H, 2-H), 10.41 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, [D$_6$]DMSO): δ = 105.19 (C≡N), 119.04 (C), 120.04 (2 CH, 2′-, 6′-CH), 127.16 (4- or 5-CH), 127.20 (5- or 4-CH), 130.61 (2-CH), 133.10 (2 CH, 3′-, 5′-CH), 137.09 (C-3), 143.36 (C), 161.29 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3330 (NH), 3095 (NH), 2231 (C≡N), 1647 (C=O) cm^{-1}. MS (EI): m/z (%) = 229.04 (2) [M + 1]$^+$, 228 (10) [M]$^+$, 111 (100) [M – 117]$^+$. HRMS: calcd. for $C_{12}H_8N_2OS$ [M]$^+$ 228.0357; found 228.0361.

***N*-(3-Cyanophenyl)thiophene-3-carboxamide (9):** From 3-bromothiophene (163.0 mg, 1.00 mmol) and 3-aminobenzonitrile (1.40 mmol, 165.0 mg) using conditions A and after purification by column chromatography using a solvent gradient from neat petroleum ether to 50% diethyl ether/petroleum ether, compound **9** was obtained as a yellow solid (103 mg, 45%). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 166–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.49 (m, 3 H), 7.52 (dd, J = 5.2, 1.2 Hz, 1 H, 4-H), 7.87–7.89 (m, 1 H), 7.96 (br. s, 1 H, NH), 8.02–8.04 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 113.02 (C), 118.50 (C), 123.28 (CH), 124.36 (CH), 126.05 (4-CH), 127.23 (CH), 127.85 (CH), 129.43 (CH), 129.97 (CH), 136.92 (C), 138.70 (C), 161.25 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3357 (NH), 3090 (NH), 2229 (C≡N), 1661 (C=O) cm^{-1}. MS (EI): m/z (%) = 229 (4) [M + 1]$^+$, 228 (39) [M]$^+$, 111 (100) [M – 117]$^+$. HRMS: calcd. for $C_{12}H_8N_2OS$ [M]$^+$ 228.0357; found 228.0354.

***N*-(Pyridin-3-yl)thiophene-3-carboxamide (10):** From 3-bromothiophene (168 mg, 1.00 mmol) and 3-aminopyridine (132 mg, 1.40 mmol) using conditions A and after purification by column chromatography using a solvent gradient from 50% diethyl ether/petroleum ether to 50% ethyl acetate/diethyl ether, or from 3-iodothiophene (0.48 mmol, 100.0 mg) and 3-aminopyridine (1.19 mmol, 112.0 mg) using conditions B and after purification by column chromatography using a solvent gradient from 80% diethyl ether/petroleum ether to 10% ethyl acetate/diethyl ether, compound **10** was obtained as an off-white solid (30.0 mg, 15%; 60.0 mg, 55%, respectively). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 166–168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32 (dd, J = 8.4, 4.8 Hz, 1 H, 5′-H), 7.39 (dd, J = 5.2, 3.2 Hz, 1 H, 5-H), 7.55 (dd, J = 5.2, 1.4 Hz, 1 H, 4-H), 8.08 (dd, J = 3.2, 1.2 Hz, 1 H, 2-H), 8.29–8.36 (m, 2 H), 8.38 (br. s, 1 H, NH), 8.70 (d, J = 2.4 Hz, 1 H, 2′-H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 123.87 (5′-CH), 126.25 (4-CH), 127.02 (5-CH), 128.03 (CH), 129.45 (2-CH), 135.04 (C-3′), 137.00 (C-3), 141.28 (2′-CH), 145.00 (CH), 161.64 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3215 (NH), 3097 (NH), 1661 (C=O) cm^{-1}. MS (ESI): m/z (%) = 227.1667 (35) [M + Na]$^+$, 205.1667 (100) [M + H]$^+$.

***N*-(2-Chloro-5-methoxyphenyl)benzo[*b*]thiophene-3-carboxamide (11):** From 3-bromobenzo[*b*]thiophene (100 mg, 0.470 mmol) and 2-chloro-5-methoxyaniline hydrochloride (127 mg, 0.660 mmol) using conditions A and after purification by column chromatog-

raphy using a solvent gradient from neat petroleum ether to 10% diethyl ether/petroleum ether, compound **11** was obtained as a yellow solid (44.0 mg, 30%). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 116–118 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 6.68 (dd, J = 9.0, 3.0 Hz, 1 H, 4′-H), 7.31 (d, J = 9.0 Hz, 1 H, 3′-H), 7.43–7.55 (m, 2 H, 5-, 6-H), 7.93 (d, J = 8.1 Hz, 1 H, 4- or 7-H), 8.09 (s, 1 H, 2-H), 8.30 (d, J = 3.0 Hz, 1 H, 6′-H), 8.34 (br. s, 1 H, NH), 8.51 (d, J = 8.1 Hz, 1 H, 4- or 7 H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.68 (OCH_3), 106.33 (6′-CH), 111.37 (4′-CH), 113.94 (C), 122.68 (4- or 7-CH), 124.18 (7- or 4-CH), 125.42 (6- or 5-CH), 125.47 (5- or 6-CH), 129.23 (C-3′), 130.46 (2-CH), 132.00 (C), 135.30 (C), 136.44 (C), 140.35 (C), 159.06 (5′-C), 161.58 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3291 (NH), 3078 (NH), 1650 (C=O) cm^{-1}. MS (EI): *m*/*z* (%) = 319.03 (2) [M, ^{37}Cl]$^+$, 317.03 (5) [M, ^{35}Cl]$^+$, 282.06 (48) [M – Cl]$^+$, 161.00 (100) [M – 156]$^+$. HRMS: calcd. for $C_{16}H_{12}ClNO_2S$ [M, ^{37}Cl] 319.0248, [M, ^{35}Cl] 317.0277; found 319.0262, 317.0273.

***N*-(2-Bromophenyl)-4-methoxybenzamide (12):** From 4-iodoanisole (100 mg, 0.430 mmol) and 2-bromoaniline (184 mg, 1.07 mmol) using conditions B and after purification by column chromatography using a solvent gradient from neat petroleum ether to 100% diethyl ether, compound **12** was obtained as a yellow solid (94.0 mg, 72%). Recrystallization from diethyl ether/petroleum ether gave pale-yellow crystals, m.p. 141–143 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, OCH_3), 6.98–7.04 (m, 3 H, 3-, 5-, 5′-H), 7.37 (m, 1 H, 4′-H), 7.58 (dd, J = 8.0, 1.5 Hz, 1 H, 6′-H), 7.92 (d, J = 8.7 Hz, 2 H, 2-, 6-H), 8.41 (br. s, 1 H, NH), 8.55 (dd, J = 8.3, 1.8 Hz, 1 H, 3′-H) ppm. ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 55.48 (OCH_3), 113.59 (C-1'), 114.12 (2 CH, 3-, 5-CH), 121.61 (3′-CH), 124.97 (5′-CH), 126.76 (C-1), 128.51 (4′-CH), 128.99 (2 CH, 2-, 6-CH), 132.18 (6′-CH), 135.97 (C-Br), 162.75 (C-4), 164.75 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3273 (NH), 1649 (C=O) cm^{-1}. MS (EI): *m*/*z* (%) = 307.01 (2) [M, ^{81}Br]$^+$, 305.01 (2) [M, ^{79}Br]$^+$, 226.09 (20) [M – Br]$^+$, 135.04 (100) [M – C_6H_5BrN]$^+$. HRMS: calcd. for $C_{14}H_{12}BrNO_2$ [M, ^{81}Br] 307.0031, [M, ^{79}Br] 305.0051; found 307.0034, 305.0045.

4-Methoxy-*N*-(pyridin-2-yl)benzamide (13): From 4-iodoanisole (100 mg, 0.430 mmol) and 2-aminopyridine (101 mg, 1.07 mmol) using conditions B and after purification by column chromatography using a solvent gradient from neat petroleum ether to 80% diethyl ether/petroleum ether, compound **13** was obtained as a yellow solid (74.0 mg, 76%). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 106–107 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 6.99 (d, J = 8.8 Hz, 2 H, 3-, 5-H), 7.04–7.07 (m, 1 H), 7.73–7.77 (m, 1 H), 7.91 (d, J = 8.8 Hz, 2 H, 2-, 6-H), 8.27–8.28 (m, 1 H), 8.38 (m, 1 H, 3′-H), 8.63 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 55.47 (OCH_3), 114.02 (3 CH, 3-, 5-, 3′-CH), 119.69 (CH), 126.42 (C-1), 129.13 (2 CH, 2, 6-CH), 138.39 (CH), 147.85 (CH), 151.74 (C), 162.80 (C-4), 165.16 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3275 (NH), 1674 (C=O) cm^{-1}. MS (EI): *m*/*z* (%) = 229.09 (1) [M + 1]$^+$, 228.09 (8) [M]$^+$, 200.09 (14) [M – 28]$^+$, 199.09 (15) [M – 29]$^+$, 135.04 (100) [M – 170]$^+$. HRMS: calcd. for $C_{13}H_{12}N_2O_2$ [M]$^+$ 228.0899; found 228.0904.

4-Methoxy-*N*-(5-methylpyridin-2-yl)benzamide (14): From 4-iodoanisole (100 mg, 0.430 mmol) and 2-amino-3-bromo-5-methylpyridine (200 mg, 1.07 mmol) using conditions B and after purification by column chromatography using a solvent gradient from neat petroleum ether to 80% diethyl ether/petroleum ether, compound **14** was obtained as a yellow solid (26.0 mg, 25%). Recrystallization from diethyl ether/petroleum ether gave yellow crystals, m.p. 112–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 3.87 (s, 3 H, OCH_3), 6.98 (d, J = 8.8 Hz, 2 H, 3-, 5-H), 7.60–7.63 (m, 1 H, 4′-H), 7.94 (d, J = 8.8 Hz, 2 H, 2-, 6-H), 8.07 (m, 1 H, 6′-H), 8.35 (d, J = 8.8 Hz, 1 H, 3′-H), 9.03 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 17.78 (CH_3), 55.45 (OCH_3), 114.00 (3 CH, 3-, 5-, 3′-CH), 126.19 (C-1), 129.10 (5′-C), 129.29 (2 CH, 2-, 6-CH), 139.95 (4′-CH), 146.18 (6′-CH), 149.37 (C-2'), 162.85 (C-4), 165.11 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3236 (NH), 1674 (C=O) cm^{-1}. MS (EI): *m*/*z* (%) = 243.11 (2) [M + H]$^+$, 242.11 (15) [M]$^+$, 214.11 (31) [M – 28]$^+$, 135.03 (100) [M – $C_6H_7N_2$]$^+$. HRMS: calcd. for $C_{14}H_{14}N_2O_2$ [M]$^+$ 242.1055; found 242.1063.

***N*-(Pyridin-2-yl)thiophene-3-carboxamide (15):** From 3-iodothiophene (100 mg, 0.480 mmol) and 2-aminopyridine (112 mg, 1.19 mmol) using conditions B and after purification by column chromatography using a solvent gradient from 80% diethyl ether/petroleum ether to 10% ethyl acetate/diethyl ether, compound **15** was obtained as a beige solid (45.0 mg, 44%). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 180–182 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02–7.06 (m, 1 H), 7.37 (dd, J = 5.2, 3.0 Hz, 1 H, 5-H), 7.56 (dd, J = 5.2, 1.2 Hz, 1 H, 4-H), 7.72–7.76 (m, 1 H), 8.07–8.08 (m, 1 H), 8.19–8.21 (m, 1 H), 8.36–8.38 (m, 1 H, 3′-H), 9.06 (br. s, 1 H, NH) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 114.44 (3′-CH), 119.76 (CH), 126.34 (4-CH), 126.81 (5-CH), 129.50 (2-CH), 137.24 (C-3), 138.58 (CH), 147.50 (CH), 151.52 (C-2'), 161.16 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3232 (NH), 3108 (NH), 1674 (C=O) cm^{-1}. MS (ESI): *m*/*z* (%) = 227.1667 (100) [M + Na]$^+$, 205.1667 (31) [M + H]$^+$.

2-(4-Methoxyphenyl)isoindoline-1,3-dione (16): From methyl 2-iodobenzoate (157 mg, 0.600 mmol) and *p*-anisidine (185 mg, 1.50 mmol) using modified conditions B (Table 6) in dry toluene and after purification by column chromatography using a solvent gradient from neat petroleum ether to 50% diethyl ether/petroleum ether, compound **16** was obtained as a beige solid (53.0 mg, 35%). Recrystallization from diethyl ether/petroleum ether gave off-white crystals, m.p. 157–159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 7.03 (d, J = 9.0 Hz, 2 H, 3′-, 5′-H), 7.35 (d, J = 9.0 Hz, 2 H, 2′-, 6′-H), 7.78–7.80 (m, 2 H), 7.95–7.97 (m, 2 H) ppm. ^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 55.50 (OCH_3), 114.48 (2 CH, 3'-, 5′-CH), 123.66 (2 CH), 124.26 (C-1'), 127.93 (2 CH, 2'-, 6′-CH), 131.84 (2 C), 134.29 (2 CH), 159.26 (C-4'), 167.56 (2 C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 1709 (C=O) cm^{-1}. MS (EI): *m*/*z* (%) = 254 (15) [M + 1]$^+$, 253 (100) [M]$^+$, 238 (60) [M – 15]$^+$, 210 (24) [M – 43]$^+$. HRMS: calcd. for $C_{15}H_{11}NO_3$ [M]$^+$ 253.0739; found 253.0744.

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[1] J. Tsuji, *Palladium Reagents and Catalysis*, Wiley, Chichester, **1995**.
[2] J. Tsuji, *Palladium Reagents and Catalysts, New Perspectives for the 21st Century*, Wiley, Chichester, **2004**.
[3] P. J. Tambade, Y. P. Patil, M. J. Bhanushali, B. M. Bhamage, *Synthesis* **2008**, 2347–2352.
[4] A. Takács, B. Jakab, A. Petz, L. Kollár, *Tetrahedron* **2007**, *63*, 10372–10378.

[5] N.-F. K. Kaiser, A. Hallberg, M. Larhed, *J. Comb. Chem.* **2002**, *4*, 109–111.
[6] J. Wannberg, M. Larhed, *J. Org. Chem.* **2003**, *68*, 5750–5753.
[7] M. A. Letavic, K. S. Ly, *Tetrahedron Lett.* **2007**, *48*, 2339–2343.
[8] K. Yamazaki, Y. Kondo, *J. Comb. Chem.* **2004**, *6*, 121–125.
[9] M. Iizuka, Y. Kondo, *Chem. Commun.* **2006**, 1739–1741.
[10] M. Iizuka, Y. Kondo, *Eur. J. Org. Chem.* **2007**, 5180–5182.
[11] V. P. W. Böhm, W. A. Herrmann, *Chem. Eur. J.* **2001**, *7*, 4191–4197.
[12] A. N. Trzeciak, J. J. Ziólkowski, *Coord. Chem. Rev.* **2005**, *249*, 2308–2322.
[13] C. F. J. Barnard, *Org. Process Res. Dev.* **2008**, *12*, 566–574.
[14] S. A. Worlikar, R. C. Larock, *J. Org. Chem.* **2008**, *73*, 7175–7180.

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