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# Palladium-Catalyzed Direct Arylations of Five-Membered Heteroarenes Bearing *N*-Monoalkylcarboxamide Substituents

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The palladium-catalyzed direct arylation of furan, thiophene, pyrrole, or pyrazole derivatives bearing CONHR substituents on C2, C3, or C5 with aryl bromides was studied. The use of KOAc as the base, DMAc as the solvent, and $PdCl(C_3H_5)$-(dppb) as the catalyst was found to give regioselectively and without decarbamoylation the arylated heteroaromatics. Under these conditions, the amide substituent on the heteroaromatic does not act as a directing group. A wide range of functional groups such as acetyl, formyl, ester, nitrile, trifluoromethyl, and fluoro on the aryl bromide is tolerated.

## Introduction

The easy access to a variety of heteroaromatics bearing functional groups such as amides is an important field for research in organic chemistry due to the biological properties of some of these derivatives. For example, Oxacillin and its derivatives are used as antibiotics, Atorvastatin is employed against cholesterol, and Rimonabant is an anorectic antiobesity drug (Figure 1).[1]

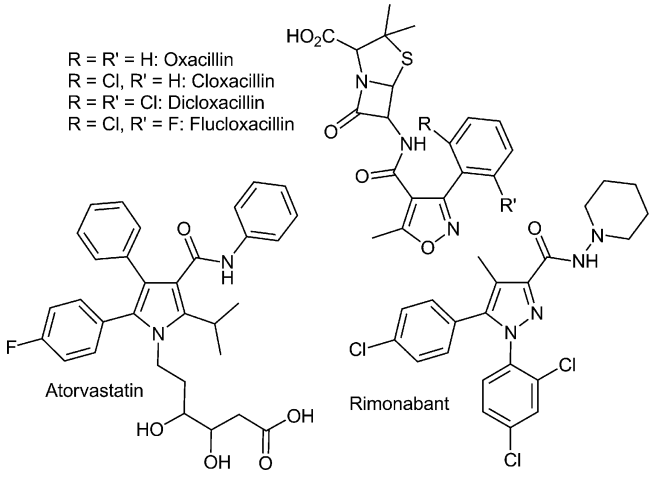


Figure 1. Examples of bioactive derivatives.

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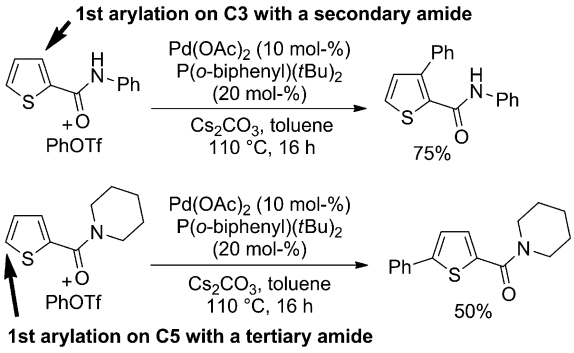
The classical palladium-catalyzed reactions such as Stille, Suzuki, or Negishi couplings allow the formation of a wide variety of biaryls.[2] However, for these couplings, the preliminary synthesis of organometallic derivatives is required. Moreover, these reactions provide a stoichiometric amount of metallic side products, from which undesired contamination could be potentially appalling for pharmaceutical, agrochemical, and related biological applications.

In 1990, Ohta and co-workers reported that the 2- or 5-arylation of several heteroaromatics, including furans and thiophenes, with aryl halides proceed in moderate to good yields through C–H bond activation by using $Pd(PPh_3)_4$ as the catalyst.[3] Since these results, the palladium-catalyzed direct arylation of heteroaromatics with aryl halides has proved to be a very powerful method for the synthesis of a wide variety of arylated heterocycles.[4–8]

The direct arylation of quite simple furan, thiophene, or pyrrole derivatives has been largely described. On the other hand, heteroaromatics bearing amide substituents have been rarely employed.[9–11] A few thiophene derivatives substituted on C2 or C3 by an amide have been used in palladium-catalyzed direct intramolecular arylations.[10,11] The intermolecular direct arylation using a thiophene with a carboxanilide function on C2 has been reported by Miura and co-workers.[9] It is worth noting that the regioselectivity of the phenylation depends on the nature of the carboxanilide function. The initial phenylation of a thiophene substituted on C2 by CONHPh takes place preferably at the 3-position, followed by the second phenylation at the 5-position (Scheme 1, top), whereas the reaction of a thiophene substituted on C2 by $CON(C_5H_{10})$ (tertiary amide) occurs in the reverse order (Scheme 1, bottom). Moreover, in some cases, the carbamoyl group was cleaved to give 2,3,5-triarylthiophenes when an excess amount of phenyl triflate was employed.[9a] With such substrates, the formation of mix-

tures of 5-arylated and 3,5-diarylated thiophenes had also been observed.[9b] Miura's group also studied the reactivity of *N*-phenyl-3-thiophenecarboxamide.[9c] This reactant was successfully triarylated on C2, C4, and C5.

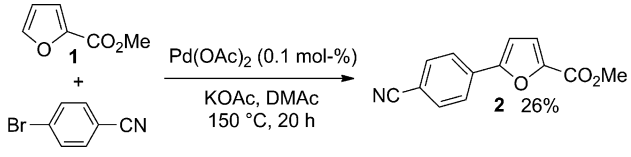



Scheme 1. Reported regioselectivity for the arylation of thiophenecarboxamides.

The palladium-catalyzed direct regioselective arylation of amide-substituted heteroaromatics should provide cost-effective and environmentally attractive access for the preparation of useful heteroaromatic derivatives. The major by-products of the reaction would be a base associated to HX, instead of metallic salts produced under more classical cross-coupling procedures[1,2] such as Suzuki, Negishi, or Stille reactions. Moreover, the method avoids the preliminary preparation of a requisite organometallic, reducing the number of steps to prepare these compounds. Herein, we wish to report on the use of amide-substituted heteroaromatics for palladium-catalyzed direct arylations, using a wide variety of electronically and sterically diverse aryl and heteroaryl bromides.

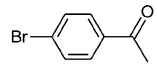
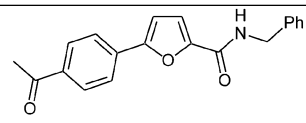
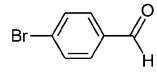
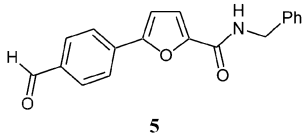
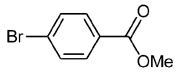
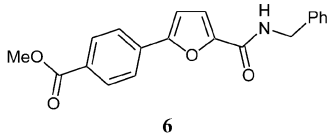
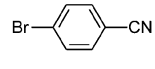
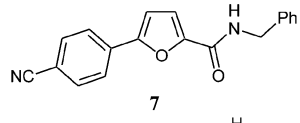
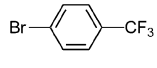
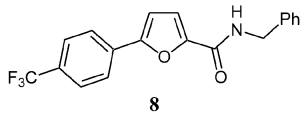
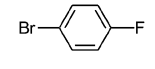
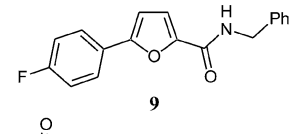
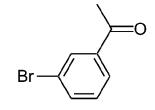
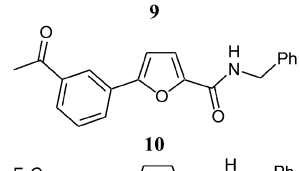
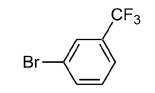
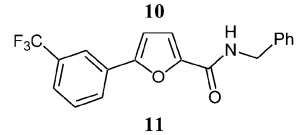
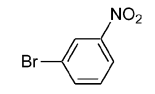
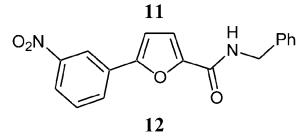
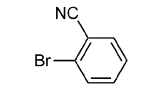
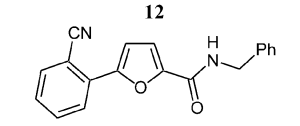
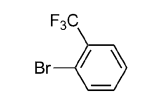
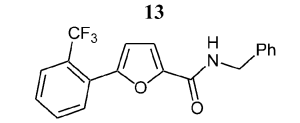
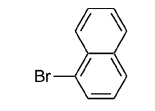
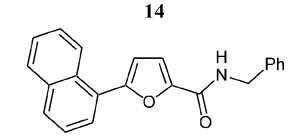
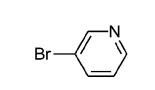
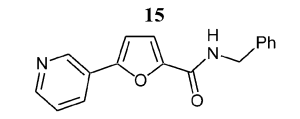
## Results and Discussion

We initially studied the reactivity of *N*-benzyl-2-furamide (**3**) with aryl bromides. We had previously observed that the coupling reaction using methyl furan-2-carboxylate (**1**) and 4-bromobenzonitrile gave the desired 5-arylated methyl furan-2-carboxylate **2** (Scheme 2).[12a] However, this compound was obtained in a low yield of 26% due to partial decarboxylation of this furan derivative. In the course of this reaction, a mixture of **2**, 2-arylfuran, and 2,5-diarylfuran was formed. Similar mixtures of products were obtained in the presence of several other aryl bromides, and shorter reaction times did not improve the yields.




Scheme 2. Coupling of methyl furan-2-carboxylate with 4-bromobenzonitrile.

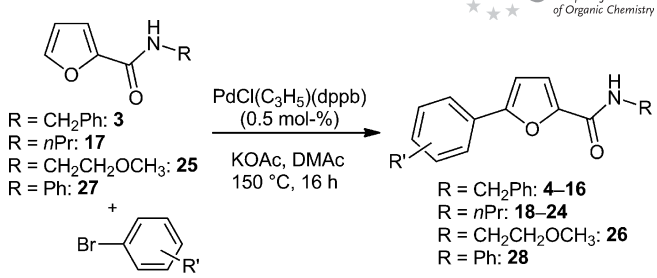
Table 1. Palladium-catalyzed coupling of *N*-benzyl-2-furamide with aryl bromides (Scheme 3).[a]

| Entry | Aryl bromide | Product | Yield [%][a] |
|---|---|---|---|
| 1 |  |  **4** | 74 |
| 2 |  |  **5** | 67 |
| 3 |  |  **6** | 87 |
| 4 |  |  **7** | 84 |
| 5 |  |  **8** | 62 |
| 6 |  |  **9** | 66 |
| 7 |  |  **10** | 81 |
| 8 |  |  **11** | 62 |
| 9 |  |  **12** | 77 |
| 10 |  |  **13** | 88 |
| 11 |  |  **14** | 80 |
| 12 |  |  **15** | 81 |
| 13 |  |  **16** | 57 |

[a] Conditions: $PdCl(C_3H_5)(dppb)$ (0.005 equiv.), *N*-benzyl-2-furamide (1.5 equiv.), aryl bromide (1 equiv.), KOAc (2 equiv.), DMAc, 150 °C, 16 h, isolated yields.

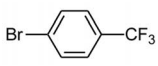
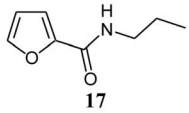
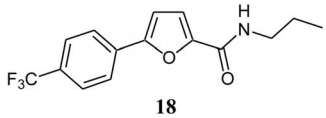
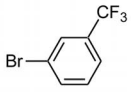
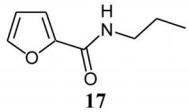
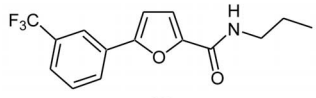
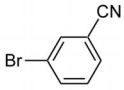
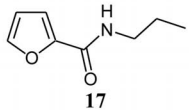
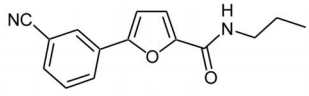
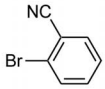
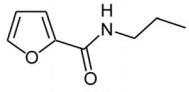
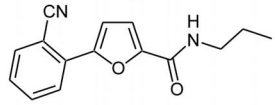
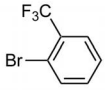
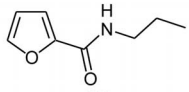
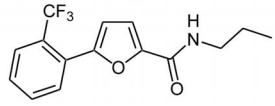
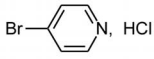
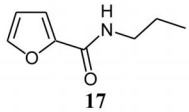
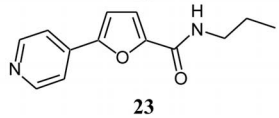
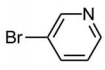
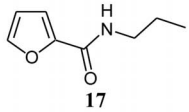
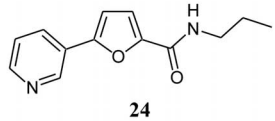
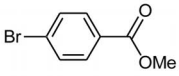
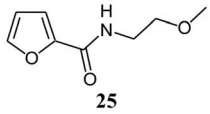
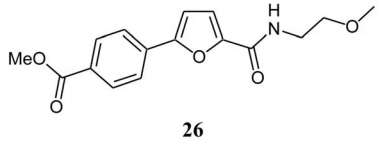
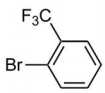
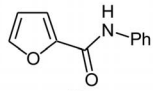
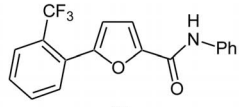
As the amide function was found to be more stable than the ester function, the yields of coupling products in the presence of **3** were higher. We observed that with KOAc as the base, and DMAc as the solvent, using only 0.5 mol-% $PdCl(C_3H_5)(dppb)$ as the catalyst, 5-arylated furans **4**–**16** were regioselectively obtained in good yields (Scheme 3, Table 1). It should be noted that under these reaction conditions, the amide substituent does not act as a directing group for the arylation, and no formation of 3-arylated furan derivatives was detected. Moreover, in the course of this reaction, no decarbamoylation by C–N fission was observed. Similar regioselectivities (arylation on C5) had been observed for the direct arylations of various heteroaromatics bearing $–CH_2NHCOR$ substituents on C2.[13]




Scheme 3. Coupling of 2-furamides with aryl bromides.

A wide range of aryl bromides was employed. In the presence of electron-deficient aryl bromides such as 4-bromoacetophenone, 4-bromobenzaldehyde, methyl 4-bromo-

Table 2. Palladium-catalyzed coupling of 2-furamide derivatives with aryl bromides (Scheme 3).

| Entry | Aryl bromide | Furan | Product | Yield [%][a] |
|---|---|---|---|---|
| 1 |  |  **17** |  **18** | 63 |
| 2 |  |  **17** |  **19** | 60 |
| 3 |  |  **17** |  **20** | 83 |
| 4 |  |  **17** |  **21** | 67 |
| 5 |  |  **17** |  **22** | 74 |
| 6 |  |  **17** |  **23** | 74 |
| 7 |  |  **17** |  **24** | 58 |
| 8 |  |  **25** |  **26** | 90 |
| 9 |  |  **27** |  **28** | 72 |

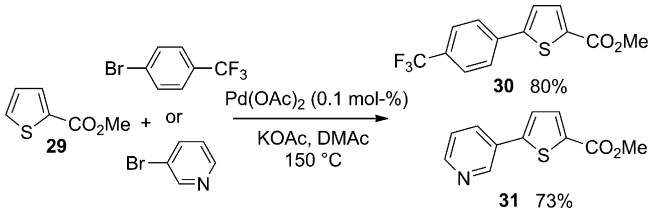
[a] Conditions: $PdCl(C_3H_5)(dppb)$ (0.005 equiv.), 2-furamide derivative (1.5 equiv.), aryl bromide (1 equiv.), KOAc (2 equiv.), DMAc, 150 °C, 16 h, isolated yields.

benzoate, 4-bromobenzonitrile, or 4-(trifluoromethyl)bromobenzene and 0.5 mol-% catalyst, products **4**–**7** were obtained in good yields (Table 1, Entries 1–5). The use of the *meta*-substituted aryl bromides 3-bromoacetophenone, 3-(trifluoromethyl)bromobenzene, and 3-bromonitrobenzene also gave 5-arylated furans **10**–**12** in good yields (Table 1, Entries 7–9). Coupling with the more-hindered substrates 2-bromobenzonitrile and 1-bromonaphthalene gave **13** and **15** in 88 and 81% yield, respectively (Table 1, Entries 10 and 12). On the other hand, in the presence of 3-bromopyridine a lower yield of 57% in **16** was obtained due to partial conversion of this aryl bromide (Table 1, Entry 13).

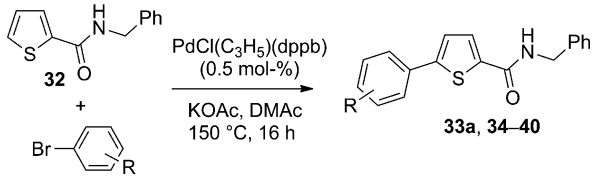
Then, the scope of this reaction for the coupling of other 2-furamides was investigated (Scheme 3, Table 2). In the presence of *N*-*n*-propyl-2-furamide (**17**) and electron-deficient aryl bromides such as 2- or 3-bromobenzonitriles or 2-, 3-, or 4-(trifluoromethyl)bromobenzenes and 0.5 mol-% catalyst, products **18**–**22** were obtained in 60–83% yield (Table 2, Entries 1–5). The use of 4-bromopyridine also gave desired product **23** in good yield (Table 2, Entry 6). The reaction of furan-2-carbonyl chloride with 2-methoxyethylamine gave substrate **25**. Arylation of **25** with methyl 4-bromobenzoate produced **26** in 90% yield (Table 2, Entry 8). Finally, the arylation of *N*-benzyl-2-furamide (**27**) with 2-(trifluoromethyl)bromobenzene also gave regioselectively the arylation at C5 to produce **28** in 72% yield (Table 2, Entry 9).

Then, we studied the reactivity of thiophene-2-carboxylic acid benzylamide (**32**). We had previously reported that, in the presence of methyl thiophene-2-carboxylate (**29**), the direct arylation proceeds nicely, and 5-arylated thiophenes **30** and **31** could be obtained in good yields without the formation of important amounts of decarboxylated products (Scheme 4).[14]



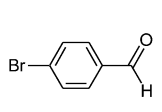
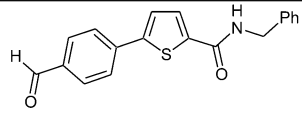
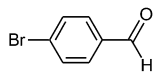
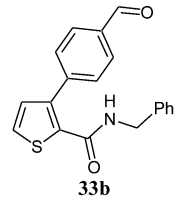
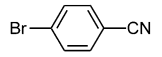
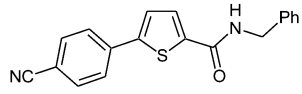
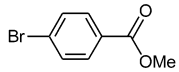
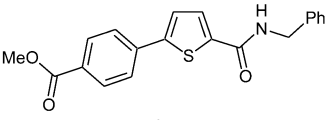
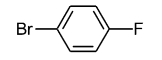
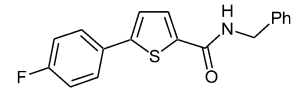
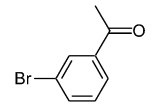
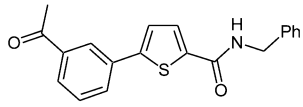
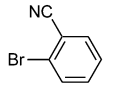
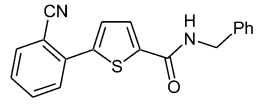
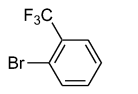
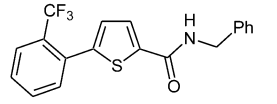
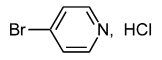
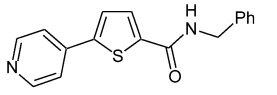

Scheme 4. Coupling of methyl thiophene-2-carboxylate with aryl bromides.

However, to determine the regioselectivity of the direct arylation of **32** under our reaction conditions, its coupling with a few aryl bromides was studied (Scheme 5, Table 3). Miura and co-workers had observed the formation of a 3-arylated thiophene when the reaction was conducted in the presence of phenyl triflate in toluene with $Cs_2CO_3$ as the base (Scheme 1, top).[9a] Using our reaction conditions, KOAc as the base, DMAc as the solvent, and 0.5 mol-% $PdCl(C_3H_5)(dppb)$ as the catalyst, only the arylation at C5 of thiophene to give products **33a** and **34**–**40** was observed. On the other hand, the use of Miura's conditions ($Cs_2CO_3$ and toluene) gave regioselectively **33b** in 66% yield (Table 3, Entry 2). The formation of C3-arylated products observed




Scheme 5. Coupling of thiophene-2-carboxylic acid benzylamide with aryl bromides.

Table 3. Palladium catalyzed coupling of thiophene-2-carboxylic acid benzylamide with aryl bromides (Scheme 5).

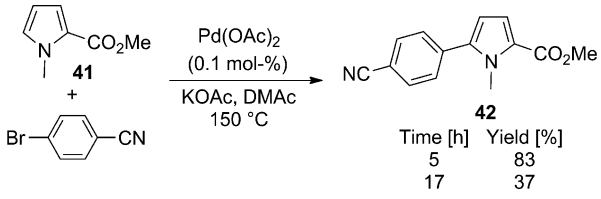
| Entry | Aryl bromide | Product | Yield [%][a] |
|---|---|---|---|
| 1 |  |  **33a** | 88 |
| 2 |  |  **33b** | 66[b] |
| 3 |  |  **34** | 72 |
| 4 |  |  **35** | 81 |
| 5 |  |  **36** | 66 |
| 6 |  |  **37** | 72 |
| 7 |  |  **38** | 71 |
| 8 |  |  **39** | 75 |
| 9 |  |  **40** | 78 |

[a] Conditions: $PdCl(C_3H_5)(dppb)$ (0.005 equiv.), thiophene-2-carboxylic acid benzylamide (1.5 equiv.), aryl bromide (1 equiv.), KOAc (2 equiv.), DMAc, 150 °C, 16 h, isolated yields. [b] $Cs_2CO_3$ (2 equiv.), toluene, 110 °C.

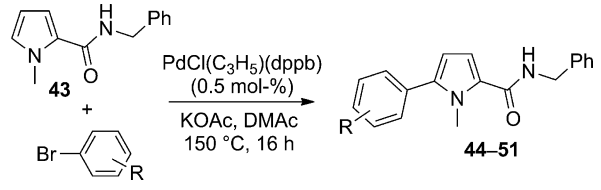
with secondary amides in the presence of $Cs_2CO_3$ as the base (Scheme 1) probably comes from a coordination-assisted mechanism.[9] On the other hand, when KOAc is employed as the base, the reaction probably proceeds through a concerted-metalation–deprotonation mechanism (CMD) to give arylation at C5.[15]

Next, we examined the reactivity of an amide-substituted pyrrole. We previously observed that for coupling reactions of aryl bromides with methyl 1-methyl-2-pyrrolecarboxylate, mixtures of the 5-arylated pyrroles and 2-arylpyrroles arising from decarboxylation were obtained when the reactions were stopped after 17 h. Up to 50% of these decarboxylated pyrroles could be formed. As this decarboxylation process was found to be relatively slow, as compared to the palladium-catalyzed 5-arylation rate, when the reactions were stopped after 2–5 h, the target products could be obtained in moderate to high yields (Scheme 6).[16b]




Scheme 6. Coupling of methyl *N*-methylpyrrole-2-carboxylate with 4-bromobenzonitrile.

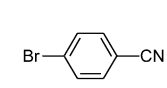
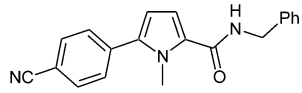
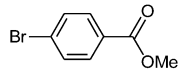
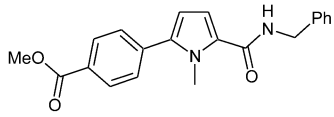
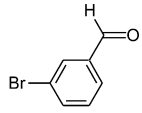
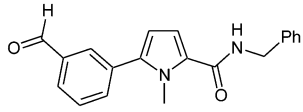
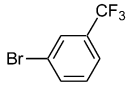
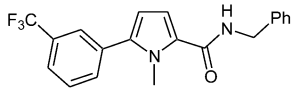
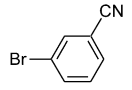
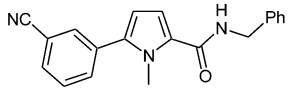
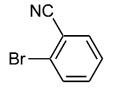
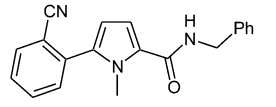
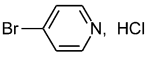
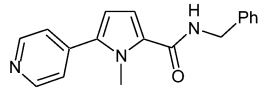
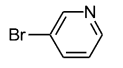
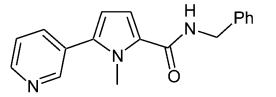
Therefore, to have more reliable access to arylpyrroles substituted by amides, we examined the direct arylation of 1-methylpyrrole-2-carboxylic acid benzylamide (**43**) with various aryl bromides (Scheme 7, Table 4). Again, the reaction was found to be very regioselective, as only the C5 arylation products were isolated. The amide function was found to be much more stable than the ester, as no decarbamoylation was detected. The reaction of 2-, 3-, or 4-bromobenzonitriles, 3-(trifluoromethyl)bromobenzene, methyl 4-bromobenzoate, or 3- or 4-bromopyridine gave the desired coupling products **44**, **45**, **47**–**51** in 70–78% yield (Table 4, Entries 1, 2, and 4–8). In the presence of 3-bromobenzaldehyde the formation of unidentified side products was observed and **46** was obtained in only 48% yield (Table 4, Entry 3).



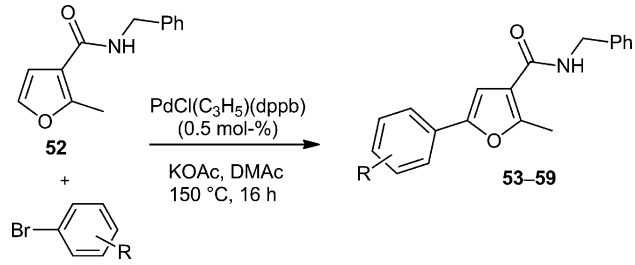

Scheme 7. Coupling of 1-methylpyrrole-2-carboxylic acid benzylamide with aryl bromides.

We also employed a furan substituted by an amide on C3 (Scheme 8, Table 5). The arylations proceed nicely with a variety of aryl bromides, and expected products **53**–**59** were obtained in good yields in all cases. Again, no formation of other isomers or decarbamoylated products was detected.

Table 4. Palladium-catalyzed coupling of 1-methylpyrrole-2-carboxylic acid benzylamide with aryl bromides (Scheme 7).

| Entry | Aryl bromide | Product | Yield [%][a] |
|---|---|---|---|
| 1 |  |  **44** | 75 |
| 2 |  |  **45** | 73 |
| 3 |  |  **46** | 48 |
| 4 |  |  **47** | 70 |
| 5 |  |  **48** | 76 |
| 6 |  |  **49** | 72 |
| 7 |  |  **50** | 78 |
| 8 |  |  **51** | **74** |

[a] Conditions: $PdCl(C_3H_5)(dppb)$ (0.005 equiv.), 1-methylpyrrole-2-carboxylic acid benzylamide (1.5 equiv.), aryl bromide (1 equiv.), KOAc (2 equiv.), DMAc, 150 °C, 16 h, isolated yields.

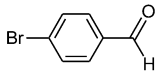
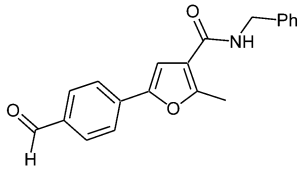
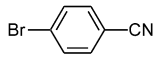
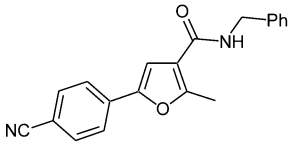
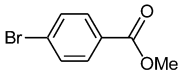
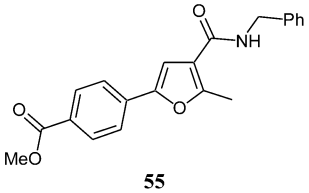
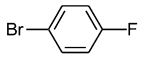
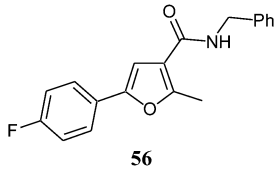
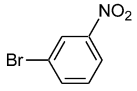
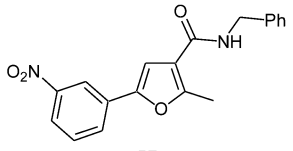
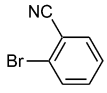
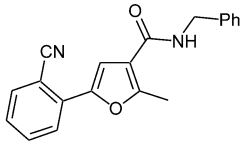
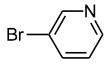
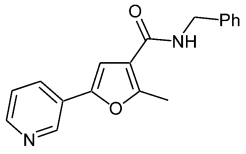



Scheme 8. Coupling of 2-methylfuran-3-carboxylic acid benzylamide with aryl bromides.

Finally, we examined the reactivity of a pyrazole substituted on the 5-position by an amide (Scheme 10). We had previously observed that when using ester-substituted pyrazole **60** in the presence of $Pd(OAc)_2/P(Ad)_2nBu$ as the cat-

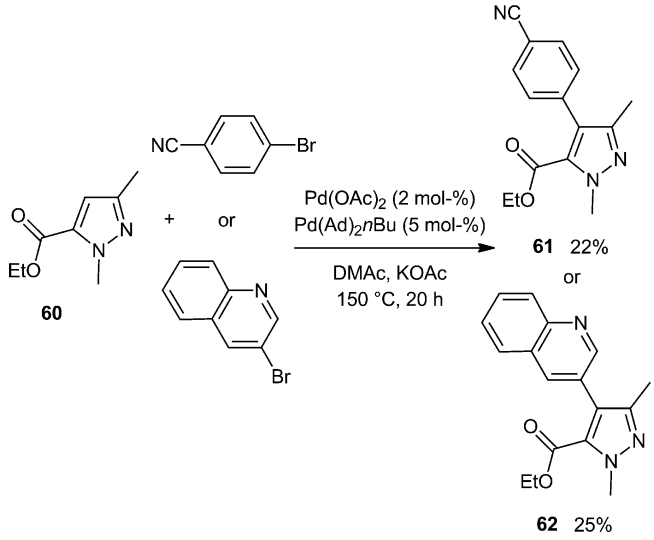
Table 5. Palladium-catalyzed coupling of 2-methylfuran-3-carboxylic acid benzylamide with aryl bromides (Scheme 8).

| Entry | Aryl bromide | Product | Yield [%][a] |
|---|---|---|---|
| 1 |  |  **53** | 68 |
| 2 |  |  **54** | 78 |
| 3 |  |  **55** | 67 |
| 4 |  |  **56** | 71 |
| 5 |  |  **57** | 72 |
| 6 |  |  **58** | 85 |
| 7 |  |  **59** | 78 |

[a] Conditions: $PdCl(C_3H_5)(dppb)$ (0.005 equiv.), 2-methylfuran-3-carboxylic acid benzylamide (1.5 equiv.), aryl bromide (1 equiv.), KOAc (2 equiv.), DMAc, 150 °C, 20 h, isolated yields.

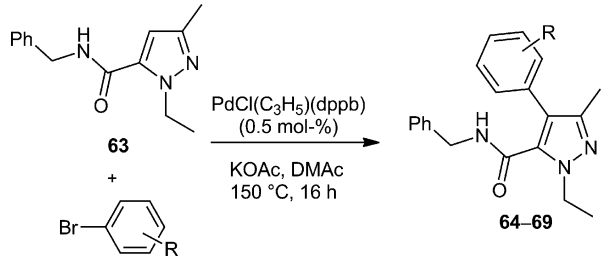
alyst, 4-arylated products **61** and **62** were obtained in very low yields (Scheme 9).[17b]

To the best of our knowledge, no example of palladium-catalyzed direct arylation of amide-substituted pyrazoles has been reported so far. Again, we observed that the use of amide-substituted compound **63** gave better yields than the use of corresponding ester-substituted pyrazole **60** (Schemes 9 and 10, Table 6). Desired coupling products **64**–




Scheme 9. Coupling of ethyl 1,3-dimethylpyrazole-5-carboxylate with aryl bromides.

**69** were obtained in good yields using *para*-, *meta*-, or *ortho*-substituted aryl bromides and an heteroaryl bromide in the presence of only 0.5 mol-% of $PdCl(C_3H_5)(dppb)$ as the catalyst.



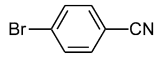
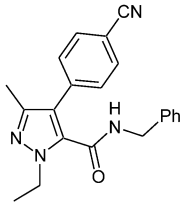
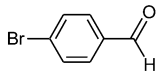
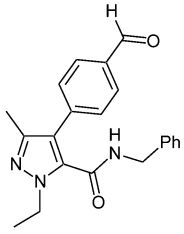
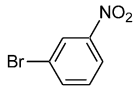
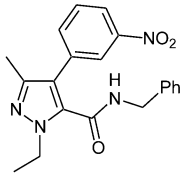
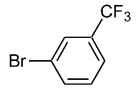
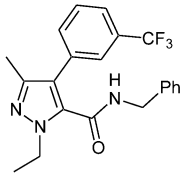
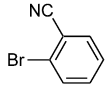
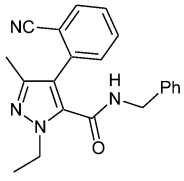
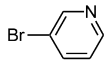
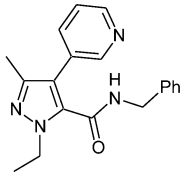

Scheme 10. Coupling of 1-ethyl-3-methylpyrazole-5-carboxylic acid benzylamide with aryl bromides.

## Conclusions

In conclusion, these results demonstrate that several heteroaromatics substituted by CONHR groups on C2, C3, or C5 can be employed for palladium-catalyzed direct arylations. Amide functions appear to be more stable than ester functions, as no decarbamoylation was observed in the course of these reactions. Therefore, for the synthesis of arylated amide-substituted heteroaromatics by palladium-catalyzed direct arylations, the preliminary transformation of esters into amides should be preferred. A low catalyst loading (0.5 mol-%) gave regioselectively the arylated compounds. It should be noted that in the presence of thiophene-2-carboxylic acid benzylamide, the 3-arylation products were not detected. When DMAc was employed as the solvent and KOAc as the base, the amide substituent on the heteroaromatics did not act as a directing group for the direct arylation. A wide range of functions such as acetyl, formyl, ester, nitrile, trifluoromethyl, and fluoro on the aryl bromide is tolerated. The major byproducts of these cou-

Table 6. Palladium-catalyzed coupling of 1-ethyl-3-methylpyrazole-5-carboxylic acid benzylamide with aryl bromides (Scheme 10).

| Entry | Aryl bromide | Product | Yield [%][a] |
|---|---|---|---|
| 1 |  |  **64** | 78 |
| 2 |  |  **65** | 76 |
| 3 |  |  **66** | 82 |
| 4 |  |  **67** | 71 |
| 5 |  |  **68** | 80 |
| 6 |  |  **69** | **74** |

[a] Conditions: $PdCl(C_3H_5)(dppb)$ (0.005 equiv.), 1-ethyl-3-methylpyrazole-5-carboxylic acid benzylamide (1.5 equiv.), aryl bromide (1 equiv.), KOAc (2 equiv.), DMAc, 150 °C, 16 h, isolated yields.

plings are AcOH/KBr instead of metallic salts with more classical coupling procedures. For these reasons, this reaction should give economically viable and environmentally attractive access to arylated amide-substituted heteroaromatics.

## Experimental Section

**General Methods**: DMAc (99%) was purchased from Acros. $[Pd(C_3H_5)Cl]_2$, 1,4-bis(diphenylphosphanyl)butane (98%), and KOAc (99%) were purchased from Alfa Aesar. These compounds were not purified before use. $^1H$ and $^{13}C$ NMR spectra were recorded with a Bruker 300 MHz spectrometer.

**Preparation of the $PdCl(C_3H_5)(dppb)$ Catalyst:** An oven-dried, 40-mL Schlenk tube equipped with a magnetic stirring bar under an argon atmosphere was charged with $[Pd(C_3H_5)Cl]_2$ (182 mg, 0.5 mmol) and dppb (426 mg, 1 mmol). Anhydrous dichloromethane (10 mL) was added, and then the solution was stirred at room temperature for 20 min. The solvent was removed in vacuo. The yellow powder was used without purification. $^{31}P$ NMR (81 MHz, $CDCl_3$) $\delta$ = 19.3 (s) ppm.

**General Procedure for Direct Arylation Reactions:** In a typical experiment, the aryl bromide (1 mmol), heteroaryl derivative (1.5 mmol), KOAc (0.196 g, 2 mmol), and $PdCl(C_3H_5)(dppb)$ (3.4 mg, 0.005 mmol) were dissolved in DMAc (4 mL) under an argon atmosphere. The reaction mixture was stirred at 150 °C for 16 h. Then, the solvent was evaporated, and the product was purified by silica gel column chromatography.

***N*-Benzyl-2-furamide (3):**[18] The reaction of furan-2-carbonyl chloride (0.312 g, 2.4 mmol), benzylamine (0.214 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **3** in 75% (0.302 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.40–7.20 (m, 6 H), 7.18 (d, $J$ = 3.0 Hz, 1 H), 6.85–6.70 (m, 1 H), 6.55–6.45 (m, 1 H), 4.67 (d, $J$ = 5.7 Hz, 2 H) ppm.

**5-(4-Acetylphenyl)furan-2-carboxylic Acid Benzylamide (4):** 4-Bromoacetophenone (0.199 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **4** in 74% (0.236 g) yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.96 (d, $J$ = 8.3 Hz, 2 H), 7.72 (d, $J$ = 8.3 Hz, 2 H), 7.40–7.20 (m, 6 H), 6.88 (d, $J$ = 3.0 Hz, 1 H), 6.85–6.75 (m, 1 H), 4.67 (d, $J$ = 5.7 Hz, 2 H), 2.62 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 196.2, 157.1, 153.1, 146.8, 136.9, 135.5, 132.5, 127.9, 127.8, 126.9, 126.7, 123.3, 115.7, 108.5, 42.2, 25.6 ppm. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37; found C 75.01, H 5.20.

**5-(4-Formylphenyl)furan-2-carboxylic Acid Benzylamide (5):** 4-Bromobenzaldehyde (0.185 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **5** in 67% (0.204 g) yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 9.97 (s, 1 H), 7.90 (d, $J$ = 8.3 Hz, 2 H), 7.72 (d, $J$ = 8.3 Hz, 2 H), 7.47 (d, $J$ = 3.8 Hz, 1 H), 7.40–7.20 (m, 6 H), 6.40–6.25 (m, 1 H), 4.60 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 191.9, 158.5, 154.3, 148.5, 138.4, 136.1, 135.2, 130.7, 129.2, 128.4, 128.1, 125.1, 117.2, 110.5, 43.7 ppm. $C_{19}H_{15}NO_3$ (305.33): calcd. C 74.74, H 4.95; found C 74.71, H 4.80.

**Methyl 4-(5-Benzylcarbamoylfuran-2-yl)benzoate (6):** Methyl 4-bromobenzoate (0.215 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **6** in 87% (0.291 g) yield. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ = 7.98 (d, $J$ = 8.3 Hz, 2 H), 7.69 (d, $J$ = 8.3 Hz, 2 H), 7.40–7.20 (m, 5 H), 7.22 (d, $J$ = 3.6 Hz, 1 H), 6.80 (d, $J$ = 3.6 Hz, 1 H), 6.80–6.75 (m, 1 H), 4.67 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 3 H) ppm. $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ = 166.9, 158.5, 154.6, 148.1, 138.4, 133.9, 130.6, 130.2, 129.2, 128.4, 128.1, 124.6, 117.1, 109.7, 52.7, 43.7 ppm. $C_{20}H_{17}NO_4$ (335.35): calcd. C 71.63, H 5.11; found C 71.50, H 5.04.

**5-(4-Cyanophenyl)furan-2-carboxylic Acid Benzylamide (7):** 4-Bromobenzonitrile (0.182 g, 1 mmol), **3** (0.302 g, 1.5 mmol), and

KOAc (0.196 g, 2 mmol) afforded **7** in 84% (0.254 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.74 (d, $J$ = 8.3 Hz, 2 H), 7.58 (d, $J$ = 8.3 Hz, 2 H), 7.40–7.20 (m, 6 H), 6.90–6.80 (m, 2 H), 4.67 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.4, 153.6, 148.6, 138.3, 133.8, 133.1, 129.2, 128.2, 128.1, 125.1, 118.9, 117.1, 112.0, 110.5, 43.6 ppm. $C_{19}H_{14}N_2O_2$ (302.33): calcd. C 75.48, H 4.67; found C 75.31, H 4.60.

**5-(4-Trifluoromethylphenyl)furan-2-carboxylic Acid Benzylamide (8):** 4-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol), **3** (0.302 g, 1.5 mmol), and KOAc (0.196 g, 2 mmol) afforded **8** in 62% (0.214 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.76 (d, $J$ = 8.3 Hz, 2 H), 7.60 (d, $J$ = 8.3 Hz, 2 H), 7.40–7.20 (m, 5 H), 7.18 (d, $J$ = 3.6 Hz, 1 H), 6.80 (d, $J$ = 3.6 Hz, 1 H), 6.80–6.75 (m, 1 H), 4.68 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 157.1, 152.7, 146.7, 136.9, 131.7, 129.2 (q, $J$ = 32.8 Hz), 127.8, 126.9, 126.7, 124.9 (q, $J$ = 3.8 Hz), 123.5, 122.8 (q, $J$ = 272.6 Hz), 115.7, 108.1, 42.2 ppm. $C_{19}H_{14}F_3NO_2$ (345.32): calcd. C 66.09, H 4.09; found C 66.10, H 4.04.

**5-(4-Fluorophenyl)furan-2-carboxylic Acid Benzylamide (9):** 4-Bromofluorobenzene (0.175 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **9** in 66% (0.195 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.77 (dd, $J$ = 8.5, 5.5 Hz, 2 H), 7.40–7.20 (m, 5 H), 7.18 (d, $J$ = 3.6 Hz, 1 H), 7.02 (t, $J$ = 8.5 Hz, 2 H), 6.80–6.70 (m, 1 H), 6.67 (d, $J$ = 3.6 Hz, 1 H), 4.68 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.8 (d, $J$ = 249.1 Hz), 157.3, 153.5, 145.8, 137.1, 127.7, 126.9, 126.6, 125.3 (d, $J$ = 8.3 Hz), 124.9, 115.6, 114.9 (d, $J$ = 21.9 Hz), 106.0, 42.1 ppm. $C_{18}H_{14}FNO_2$ (295.31): calcd. C 73.21, H 4.78; found C 73.08, H 4.77.

**5-(3-Acetylphenyl)furan-2-carboxylic Acid Benzylamide (10):** 3-Bromoacetophenone (0.199 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **10** in 81% (0.258 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.21 (s, 1 H), 7.80 (d, $J$ = 8.4 Hz, 2 H), 7.54 (t, $J$ = 8.4 Hz, 1 H), 7.50–7.30 (m, 5 H), 7.21 (d, $J$ = 3.6 Hz, 1 H), 6.85–6.80 (m, 1 H), 6.80 (d, $J$ = 3.6 Hz, 1 H), 4.68 (d, $J$ = 5.9 Hz, 2 H), 2.61 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 196.7, 157.2, 153.3, 146.4, 137.1, 136.6, 129.1, 128.1, 127.8, 127.7, 127.4, 126.9, 126.6, 122.8, 115.7, 107.3, 42.2, 25.7 ppm. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37; found C 75.04, H 5.27.

**5-(3-Trifluoromethylphenyl)furan-2-carboxylic Acid Benzylamide (11):** 3-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **11** in 62% (0.214 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.90–7.70 (m, 2 H), 7.60–7.20 (m, 7 H), 7.18 (d, $J$ = 3.6 Hz, 1 H), 6.80–6.75 (m, 2 H), 4.68 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 157.1, 152.7, 146.5, 130.7, 130.3 (q, $J$ = 32.5 Hz), 129.3, 128.4, 127.8, 126.9, 126.7, 126.5, 124.1 (q, $J$ = 3.6 Hz), 123.3 (q, $J$ = 272.6 Hz), 120.1 (q, $J$ = 3.9 Hz), 115.7, 107.6, 42.2 ppm. $C_{19}H_{14}F_3NO_2$ (345.32): calcd. C 66.09, H 4.09; found C 65.98, H 4.15.

**5-(3-Nitrophenyl)furan-2-carboxylic Acid Benzylamide (12):**[19] 3-Bromonitrobenzene (0.202 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **12** in 77% (0.248 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.52 (s, 1 H), 8.17 (d, $J$ = 8.4 Hz, 1 H), 7.94 (d, $J$ = 8.4 Hz, 1 H), 7.58 (t, $J$ = 8.4 Hz, 1 H), 7.50–7.20 (m, 6 H), 6.90 (d, $J$ = 3.6 Hz, 1 H), 6.80–6.70 (m, 1 H), 4.71 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 156.6, 151.4, 147.5, 146.8, 136.6, 129.9, 128.8, 128.7, 127.6, 126.8, 126.5, 121.7, 117.9, 115.5, 108.2, 42.0 ppm.

**5-(2-Cyanophenyl)furan-2-carboxylic Acid Benzylamide (13):** 2-Bromobenzonitrile (0.182 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **13** in 88% (0.266 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.78 (d, $J$ = 8.4 Hz, 1 H), 7.64 (d, $J$ = 8.4 Hz, 1 H), 7.50–7.20 (m, 9 H), 7.10 (d, $J$ = 3.6 Hz, 1 H), 4.71 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.0, 151.0, 147.8, 138.0, 134.4, 133.0, 131.8, 128.7, 128.4, 127.9, 127.6, 126.4, 119.1, 116.1, 111.4, 107.5, 43.3 ppm. $C_{19}H_{14}N_2O_2$ (302.33): calcd. C 75.48, H 4.67; found C 75.67, H 4.69.

**5-(2-Trifluoromethylphenyl)furan-2-carboxylic Acid Benzylamide (14):**[20] 2-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **14** in 80% (0.276 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.78 (d, $J$ = 8.0 Hz, 1 H), 7.68 (d, $J$ = 8.0 Hz, 1 H), 7.49 (t, $J$ = 7.7 Hz, 1 H), 7.46–7.20 (m, 7 H), 6.79 (d, $J$ = 3.6 Hz, 1 H), 6.80–6.75 (m, 1 H), 4.68 (d, $J$ = 5.9 Hz, 2 H) ppm.

**5-Naphthalen-1-ylfuran-2-carboxylic Acid Benzylamide (15):** 1-Bromonaphthalene (0.207 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **15** in 81% (0.265 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.35–8.25 (m, 1 H), 7.95–7.20 (m, 12 H), 6.98–6.80 (m, 1 H), 6.82 (d, $J$ = 3.6 Hz, 1 H), 4.69 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.8, 155.2, 149.7, 147.7, 138.5, 134.2, 130.1, 129.2, 129.1, 128.3, 128.0, 127.8, 127.5, 127.4, 126.7, 125.6, 125.4, 116.7, 112.1, 43.6 ppm. $C_{22}H_{17}NO_2$ (327.38): calcd. C 80.71, H 5.23; found C 80.60, H 4.99.

**5-Pyridin-3-ylfuran-2-carboxylic Acid Benzylamide (16):** 3-Bromopyridine (0.158 g, 1 mmol) and **3** (0.302 g, 1.5 mmol) afforded **16** in 57% (0.158 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.85 (s, 1 H), 8.48 (d, $J$ = 3.9 Hz, 1 H), 7.88 (d, $J$ = 8.0 Hz, 1 H), 7.40–7.20 (m, 7 H), 6.98–6.85 (m, 1 H), 6.73 (d, $J$ = 3.6 Hz, 1 H), 4.63 (d, $J$ = 5.9 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.5, 152.8, 149.6, 148.2, 146.2, 138.5, 131.9, 129.1, 128.3, 128.0, 126.2, 124.0, 116.8, 109.0, 43.6 ppm. $C_{17}H_{14}N_2O_2$ (278.31): calcd. C 73.37, H 5.07; found C 73.54, H 4.98.

***N*-*n*-Propyl-2-furamide (17):**[21] The reaction of furan-2-carbonyl chloride (0.312 g, 2.4 mmol) and *n*-propylamine (0.118 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **17** in 72% (0.220 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.32 (m, 1 H), 6.91 (m, 1 H), 6.90–6.70 (m, 1 H), 6.32 (m, 1 H), 3.30 (q, $J$ = 7.5 Hz, 2 H), 1.47 (sext., $J$ = 7.5 Hz, 2 H), 0.81 (t, $J$ = 7.5 Hz, 3 H) ppm.

**5-(4-Trifluoromethylphenyl)furan-2-carboxylic Acid Propylamide (18):** 4-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **17** (0.230 g, 1.5 mmol) afforded **18** in 63% (0.187 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.76 (d, $J$ = 8.3 Hz, 2 H), 7.70 (d, $J$ = 8.3 Hz, 2 H), 7.18 (d, $J$ = 3.6 Hz, 1 H), 6.81 (d, $J$ = 3.6 Hz, 1 H), 6.60–6.45 (m, 1 H), 3.39 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 157.2, 152.5, 147.0, 131.7, 126.1 (q, $J$ = 32.0 Hz), 124.9 (q, $J$ = 3.8 Hz), 123.8, 123.1 (q, $J$ = 272.6 Hz), 115.2, 108.1, 40.0, 22.0, 10.4 ppm. $C_{15}H_{14}F_3NO_2$ (297.27): calcd. C 60.60, H 4.75; found C 60.78, H 4.58.

**5-(3-Trifluoromethylphenyl)furan-2-carboxylic Acid Propylamide (19):** 3-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **17** (0.230 g, 1.5 mmol) afforded **19** in 60% (0.178 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.94 (s, 1 H), 7.88 (d, $J$ = 8.2 Hz, 1 H), 7.70–7.50 (m, 2 H), 7.19 (d, $J$ = 3.6 Hz, 1 H), 6.81 (d, $J$ = 3.6 Hz, 1 H), 6.60–6.45 (m, 1 H), 3.39 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.6, 153.9, 148.3, 130.8, 129.8, 129.7 (q, $J$ = 32.8 Hz), 127.9, 125.4 (q, $J$ = 3.8 Hz), 122.8 (q, $J$ = 272.6 Hz), 121.5 (q, $J$ = 3.8 Hz), 116.6, 109.0, 41.4, 23.5, 11.8 ppm. $C_{15}H_{14}F_3NO_2$ (297.27): calcd. C 60.60, H 4.75; found C 60.51, H 4.68.

**5-(3-Cyanophenyl)furan-2-carboxylic Acid Propylamide (20):** 3-Bromobenzonitrile (0.182 g, 1 mmol) and **17** (0.230 g, 1.5 mmol) afforded **20** in 83% (0.211 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.98 (s, 1 H), 7.90 (d, $J$ = 8.2 Hz, 1 H), 7.60–7.40 (m, 2 H), 7.19 (d, $J$ = 3.6 Hz, 1 H), 6.79 (d, $J$ = 3.6 Hz, 1 H), 6.78–6.60 (m, 1 H), 3.39 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.5, 152.9, 148.6, 131.9, 131.3, 130.1, 128.7, 128.1, 118.8, 116.5, 113.6, 109.4, 41.5, 23.4, 11.8 ppm. $C_{15}H_{14}N_2O_2$ (254.28): calcd. C 70.85, H 5.55; found C 70.99, H 5.47.

**5-(2-Cyanophenyl)furan-2-carboxylic Acid Propylamide (21):** 2-Bromobenzonitrile (0.182 g, 1 mmol), **17** (0.230 g, 1.5 mmol), and KOAc (0.196 g, 2 mmol) afforded **21** in 67% (0.170 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.78 (d, $J$ = 8.4 Hz, 1 H), 7.67 (d, $J$ = 8.4 Hz, 1 H), 7.60 (t, $J$ = 7.8 Hz, 1 H), 7.32 (t, $J$ = 7.8 Hz, 1 H), 7.14 (d, $J$ = 3.6 Hz, 1 H), 7.05 (d, $J$ = 3.6 Hz, 1 H), 6.90–6.70 (m, 1 H), 3.41 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.5, 151.2, 148.5, 134.9, 133.4, 132.2, 128.7, 126.7, 119.7, 115.9, 111.5, 107.7, 41.5, 23.2, 11.8 ppm. $C_{15}H_{14}N_2O_2$ (254.28): calcd. C 70.85, H 5.55; found C 70.91, H 5.48.

**5-(2-Trifluoromethylphenyl)furan-2-carboxylic Acid Propylamide (22):** 2-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **17** (0.230 g, 1.5 mmol) afforded **22** in 74% (0.220 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.78 (d, $J$ = 8.4 Hz, 1 H), 7.65 (d, $J$ = 8.4 Hz, 1 H), 7.61 (t, $J$ = 7.8 Hz, 1 H), 7.50 (t, $J$ = 7.8 Hz, 1 H), 7.17 (d, $J$ = 3.6 Hz, 1 H), 6.77 (d, $J$ = 3.6 Hz, 1 H), 6.60–6.40 (m, 1 H), 3.38 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 157.2, 150.9, 147.2, 130.9, 129.3, 127.8, 127.2, 126.1 (q, $J$ = 32.0 Hz), 126.0 (q, $J$ = 5.8 Hz), 123.8 (q, $J$ = 273.3 Hz), 114.3, 110.7 (q, $J$ = 2.0 Hz), 39.8, 21.8, 10.2 ppm. $C_{15}H_{14}F_3NO_2$ (297.27): calcd. C 60.60, H 4.75; found C 60.71, H 4.74.

**5-Pyridin-4-ylfuran-2-carboxylic Acid Propylamide (23):** 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) and **17** (0.230 g, 1.5 mmol) afforded **23** in 74% (0.170 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.57 (d, $J$ = 5.3 Hz, 2 H), 7.49 (d, $J$ = 5.3 Hz, 2 H), 7.16 (d, $J$ = 3.6 Hz, 1 H), 6.84 (d, $J$ = 3.6 Hz, 1 H), 6.78–6.60 (m, 1 H), 3.39 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.4, 152.5, 150.6, 149.1, 136.9, 118.6, 116.3, 111.1, 41.4, 23.4, 11.8 ppm. $C_{13}H_{14}N_2O_2$ (230.26): calcd. C 67.81, H 6.13; found C 67.60, H 6.04.

**5-Pyridin-3-ylfuran-2-carboxylic Acid Propylamide (24):** 3-Bromopyridine (0.158 g, 1 mmol) and **17** (0.230 g, 1.5 mmol) afforded **24** in 58% (0.133 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.80 (s, 1 H), 8.48 (d, $J$ = 3.9 Hz, 1 H), 7.86 (d, $J$ = 8.0 Hz, 1 H), 7.23 (dd, $J$ = 8.0, 3.9 Hz, 1 H), 7.12 (d, $J$ = 3.6 Hz, 1 H), 6.80–6.70 (m, 1 H), 6.70 (d, $J$ = 3.6 Hz, 1 H), 3.39 (q, $J$ = 7.5 Hz, 2 H), 1.62 (sext., $J$ = 7.5 Hz, 2 H), 0.98 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.6, 152.5, 149.6, 148.6, 146.1, 131.9, 126.2, 124.0, 116.3, 109.0, 41.4, 23.4, 11.8 ppm. $C_{13}H_{14}N_2O_2$ (230.26): calcd. C 67.81, H 6.13; found C 67.97, H 6.14.

**Furan-2-carboxylic Acid (2-Methoxyethyl)amide (25):** The reaction of furan-2-carbonyl chloride (0.312 g, 2.4 mmol) and 2-methoxyethylamine (0.150 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **25** in 70% (0.237 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.30–7.25 (m, 1 H), 7.00–6.80 (m, 2 H), 6.30–6.20 (m, 1 H), 3.50–3.30 (m, 4 H), 3.18 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.8, 148.4, 144.3, 114.5, 112.4, 71.5, 59.2, 39.2 ppm. $C_8H_{11}NO_3$ (169.18): calcd. C 56.80, H 6.55; found C 56.74, H 6.51.

**Methyl 4-[5-(2-Methoxyethylcarbamoyl)furan-2-yl]benzoate (26):** Methyl 4-bromobenzoate (0.215 g, 1 mmol) and **25** (0.254 g, 1.5 mmol) afforded **26** in 90% (0.273 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.16 (d, $J$ = 8.2 Hz, 2 H), 7.78 (d, $J$ = 8.2 Hz, 2 H), 7.19 (d, $J$ = 3.6 Hz, 1 H), 6.78 (d, $J$ = 3.6 Hz, 1 H), 6.75–6.60 (m, 1 H), 3.94 (s, 3 H), 3.80–3.50 (m, 4 H), 3.51 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 166.9, 158.6, 154.6, 148.2, 133.9, 130.7, 130.6, 124.6, 116.8, 109.7, 71.6, 59.4, 52.7, 39.4 ppm. $C_{16}H_{17}NO_5$ (303.31): calcd. C 63.36, H 5.65; found C 63.47, H 5.70.

***N*-Phenyl-2-furamide (27):**[22] The reaction of furan-2-carbonyl chloride (0.312 g, 2.4 mmol) and aniline (0.186 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **27** in 83% (0.155 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.25–8.15 (m, 1 H), 7.70 (d, $J$ = 8.2 Hz, 2 H), 7.50–7.05 (m, 5 H), 7.56 (d, $J$ = 3.3 Hz, 1 H) ppm.

**5-(2-Trifluoromethylphenyl)furan-2-carboxylic Acid Phenylamide (28):**[20] 2-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **27** (0.280 g, 1.5 mmol) afforded **28** in 72% (0.238 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.35–8.25 (m, 1 H), 8.00–7.00 (m, 10 H), 6.80 (d, $J$ = 3.4 Hz, 1 H) ppm.

**Thiophene-2-carboxylic Acid Benzylamide (32):**[23] The reaction of thiophene-2-carbonyl chloride (0.350 g, 2.4 mmol) and benzylamine (0.214 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **32** in 74% (0.321 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.60–7.20 (m, 7 H), 7.02 (dd, $J$ = 5.0, 3.9 Hz, 1 H), 6.60–6.40 (m, 1 H), 4.70 (d, $J$ = 5.7 Hz, 2 H) ppm.

**5-(4-Formylphenyl)thiophene-2-carboxylic Acid Benzylamide (33a):** 4-Bromobenzaldehyde (0.185 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **33a** in 88% (0.283 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.97 (s, 1 H), 7.90 (d, $J$ = 8.3 Hz, 2 H), 7.72 (d, $J$ = 8.3 Hz, 2 H), 7.47 (d, $J$ = 3.8 Hz, 1 H), 7.40–7.20 (m, 6 H), 6.40–6.25 (m, 1 H), 4.60 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 191.3, 161.3, 147.0, 139.3, 139.0, 137.8, 135.9, 130.5, 129.0, 128.9, 128.0, 127.8, 126.4, 125.2, 44.2 ppm. $C_{19}H_{15}NO_2S$ (321.39): calcd. C 71.00, H 4.70; found C 70.81, H 4.51.

**3-(4-Formylphenyl)thiophene-2-carboxylic Acid Benzylamide (33b):** 4-Bromobenzaldehyde (0.185 g, 1 mmol), **32** (0.325 g, 1.5 mmol), $PdCl(C_3H_5)$(dppb) (3.4 mg, 0.005 mmol), and $Cs_2CO_3$ (0.652 g, 2 mmol) in toluene (4 mL) at 110 °C under an argon atmosphere afforded **33b** in 66% (0.212 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.99 (s, 1 H), 7.81 (d, $J$ = 8.0 Hz, 2 H), 7.55 (d, $J$ = 8.0 Hz, 2 H), 7.50 (d, $J$ = 5.0 Hz, 1 H), 7.30–7.22 (m, 3 H), 7.15–7.05 (m, 3 H), 5.80–5.75 (m, 1 H), 4.43 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 190.4, 160.8, 140.3, 139.8, 136.2, 134.8, 134.1, 129.1, 129.0, 128.7, 127.7, 126.8, 126.6, 43.1 ppm. $C_{19}H_{15}NO_2S$ (321.39): calcd. C 71.00, H 4.70; found C 70.89, H 4.87.

**5-(4-Cyanophenyl)thiophene-2-carboxylic Acid Benzylamide (34):** 4-Bromobenzonitrile (0.182 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **34** in 72% (0.229 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.80–7.25 (m, 11 H), 6.40–6.20 (m, 1 H), 4.65 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 158.2, 143.0, 139.0,

137.4, 135.5, 131.4, 127.7, 126.7, 125.7, 125.3, 125.2, 124.7, 117.3, 109.4, 43.4 ppm. $C_{19}H_{14}N_2OS$ (318.39): calcd. C 71.67, H 4.43; found C 71.80, H 4.52.

**Methyl 4-(5-Benzylcarbamoylthiophen-2-yl)benzoate (35):** Methyl 4-bromobenzoate (0.215 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **35** in 81% (0.284 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.11 (d, $J$ = 8.4 Hz, 2 H), 7.69 (d, $J$ = 8.4 Hz, 2 H), 7.48 (d, $J$ = 3.7 Hz, 1 H), 7.40–7.20 (m, 6 H), 6.40–6.20 (m, 1 H), 4.71 (d, $J$ = 5.7 Hz, 2 H), 3.91 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 165.1, 160.1, 145.1, 139.7, 138.7, 136.8, 129.5, 128.7, 128.4, 127.7, 126.6, 126.3, 125.4, 125.1, 51.6, 41.9 ppm. $C_{20}H_{17}NO_3S$ (351.42): calcd. C 68.36, H 4.88; found C 68.22, H 4.71.

**5-(4-Fluorophenyl)thiophene-2-carboxylic Acid Benzylamide (36):** 4-Bromofluorobenzene (0.175 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **36** in 66% (0.205 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.55 (dd, $J$ = 8.4, 5.2 Hz, 2 H), 7.48 (d, $J$ = 3.7 Hz, 1 H), 7.40–7.25 (m, 5 H), 7.17 (d, $J$ = 3.7 Hz, 1 H), 7.10 (t, $J$ = 8.4 Hz, 2 H), 6.60–6.40 (m, 1 H), 4.62 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.8 (d, $J$ = 248.9 Hz), 160.6, 146.8, 136.9, 136.3, 128.0, 127.8, 127.0, 126.9, 126.7 (d, $J$ = 3.6 Hz), 122.4, 115.1 (d, $J$ = 22.0 Hz), 43.0 ppm. $C_{18}H_{14}FNOS$ (311.37): calcd. C 69.43, H 4.53; found C 69.20, H 4.40.

**5-(3-Acetylphenyl)thiophene-2-carboxylic Acid Benzylamide (37):** 3-Bromoacetophenone (0.199 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **37** in 72% (0.241 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.18 (s, 1 H), 7.91 (d, $J$ = 7.7 Hz, 1 H), 7.83 (d, $J$ = 7.8 Hz, 1 H), 7.60–7.20 (m, 8 H), 6.50–6.30 (m, 1 H), 4.63 (d, $J$ = 5.7 Hz, 2 H), 2.64 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 196.6, 160.5, 146.6, 137.1, 136.9, 136.8, 133.0, 129.4, 128.4, 128.0, 127.8, 127.2, 126.9, 126.7, 124.6, 123.2, 43.0, 25.7 ppm. $C_{20}H_{17}NO_2S$ (335.42): calcd. C 71.62, H 5.11; found C 71.39, H 5.20.

**5-(2-Cyanophenyl)thiophene-2-carboxylic Acid Benzylamide (38):** 2-Bromobenzonitrile (0.182 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **38** in 71% (0.226 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.80–7.25 (m, 11 H), 6.70–6.50 (m, 1 H), 4.62 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.8, 144.1, 140.7, 138.3, 137.0, 134.8, 133.7, 130.2, 129.2, 128.9, 128.8, 128.4, 128.3, 128.1, 118.9, 110.6, 44.5 ppm. $C_{19}H_{14}N_2OS$ (318.39): calcd. C 71.67, H 4.43; found C 71.78, H 4.32.

**5-(2-Trifluoromethylphenyl)thiophene-2-carboxylic Acid Benzylamide (39):**[20] 2-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **39** in 75% (0.271 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.78 (d, $J$ = 6.8 Hz, 1 H), 7.65–7.15 (m, 9 H), 7.07 (d, $J$ = 3.5 Hz, 1 H), 6.79 (t, $J$ = 5.7 Hz, 1 H), 4.62 (d, $J$ = 5.7 Hz, 2 H) ppm.

**5-Pyridin-4-ylthiophene-2-carboxylic Acid Benzylamide (40):** 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) and **32** (0.325 g, 1.5 mmol) afforded **40** in 78% (0.229 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.60 (d, $J$ = 4.9 Hz, 2 H), 7.60–7.15 (m, 9 H), 6.80–6.75 (m, 1 H), 4.63 (d, $J$ = 5.7 Hz, 2 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 161.0, 150.9, 144.5, 141.5, 140.3, 139.6, 129.6, 128.7, 127.7, 127.4, 127.3, 120.1, 43.0 ppm. $C_{17}H_{14}N_2OS$ (294.37): calcd. C 69.36, H 4.79; found C 69.20, H 4.82.

**1-Methylpyrrole-2-carboxylic Acid Benzylamide (43):**[24] The reaction of 1-methylpyrrole-2-carbonyl chloride (0.343 g, 2.4 mmol) and benzylamine (0.214 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **43** in 66% (0.282 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.50–7.30 (m, 5 H), 6.71 (m, 1 H), 6.54 (d, $J$ = 3.7 Hz, 1 H), 6.40–6.20 (m, 1 H), 6.05 (m, 1 H), 4.56 (d, $J$ = 5.7 Hz, 2 H), 3.92 (s, 3 H) ppm.

**5-(4-Cyanophenyl)-1-methylpyrrole-2-carboxylic Acid Benzylamide (44):** 4-Bromobenzonitrile (0.182 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **44** in 75% (0.236 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.70 (d, $J$ = 8.4 Hz, 2 H), 7.44 (d, $J$ = 8.4 Hz, 2 H), 7.40–7.20 (m, 5 H), 6.56 (d, $J$ = 3.7 Hz, 1 H), 6.50–6.40 (m, 1 H), 6.22 (d, $J$ = 3.7 Hz, 1 H), 4.55 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.8, 138.5, 138.0, 136.8, 132.3, 129.5, 128.8, 128.7, 127.7, 127.5, 118.7, 111.9, 111.1, 109.8, 43.4, 34.7 ppm. $C_{20}H_{17}N_3O$ (315.37): calcd. C 76.17, H 5.43; found C 76.40, H 5.29.

**Methyl 4-(5-Benzylcarbamoyl-1-methylpyrrol-2-yl)benzoate (45):** Methyl 4-bromobenzoate (0.215 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **45** in 73% (0.254 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.08 (d, $J$ = 8.4 Hz, 2 H), 7.46 (d, $J$ = 8.4 Hz, 2 H), 7.40–7.20 (m, 5 H), 6.57 (d, $J$ = 3.7 Hz, 1 H), 6.50–6.30 (m, 1 H), 6.22 (d, $J$ = 3.7 Hz, 1 H), 4.57 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 6 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 166.8, 161.9, 139.0, 138.6, 136.7, 129.7, 129.2, 129.0, 128.7, 128.0, 127.7, 127.5, 111.7, 109.3, 52.2, 43.4, 34.7 ppm. $C_{21}H_{20}N_2O_3$ (348.40): calcd. C 72.40, H 5.79; found C 72.38, H 5.87.

**5-(3-Formylphenyl)-1-methylpyrrole-2-carboxylic Acid Benzylamide (46):** 3-Bromobenzaldehyde (0.185 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **46** in 48% (0.151 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 10.03 (s, 1 H), 7.88 (s, 1 H), 7.84 (d, $J$ = 8.0 Hz, 1 H), 7.70–7.50 (m, 2 H), 7.40–7.20 (m, 5 H), 6.60 (d, $J$ = 3.7 Hz, 1 H), 6.40–6.30 (m, 1 H), 6.19 (d, $J$ = 3.7 Hz, 1 H), 4.57 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 191.9, 161.9, 138.6, 138.5, 136.7, 134.9, 133.4, 130.3, 129.2, 128.9, 128.7, 127.7, 127.5, 111.7, 109.0, 43.4, 34.5 ppm. $C_{20}H_{18}N_2O_2$ (318.37): calcd. C 75.45, H 5.70; found C 75.44, H 5.57.

**1-Methyl-5-(3-trifluoromethylphenyl)pyrrole-2-carboxylic Acid Benzylamide (47):** 3-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **47** in 70% (0.251 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.80–7.20 (m, 9 H), 6.67 (d, $J$ = 3.7 Hz, 1 H), 6.41 (t, $J$ = 5.7 Hz, 1 H), 6.23 (d, $J$ = 3.7 Hz, 1 H), 4.62 (d, $J$ = 5.7 Hz, 2 H), 3.92 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 162.7, 139.4, 139.3, 133.9, 133.2, 131.8 (q, $J$ = 32.0 Hz), 129.8, 129.6, 128.5, 128.3, 126.7 (q, $J$ = 3.8 Hz), 125.5 (q, $J$ = 3.8 Hz), 125.0 (q, $J$ = 272.0 Hz), 112.5, 109.8, 44.1, 35.3 ppm. $C_{20}H_{17}F_3N_2O$ (358.36): calcd. C 67.03, H 4.78; found C 67.11, H 4.64.

**5-(3-Cyanophenyl)-1-methylpyrrole-2-carboxylic Acid Benzylamide (48):** 3-Bromobenzonitrile (0.182 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **48** in 76% (0.239 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.70–7.50 (m, 4 H), 7.40–7.20 (m, 5 H), 6.61 (d, $J$ = 3.7 Hz, 1 H), 6.50–6.30 (m, 1 H), 6.18 (d, $J$ = 3.7 Hz, 1 H), 4.55 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.8, 138.5, 137.4, 133.7, 133.4, 132.5, 131.2, 129.4, 128.7, 128.1, 127.7, 127.5, 118.4, 112.9, 111.8, 109.3, 43.4, 34.5 ppm. $C_{20}H_{17}N_3O$ (315.37): calcd. C 76.17, H 5.43; found C 76.04, H 5.49.

**5-(2-Cyanophenyl)-1-methylpyrrole-2-carboxylic Acid Benzylamide (49):** 2-Bromobenzonitrile (0.182 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **49** in 72% (0.227 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.77 (d, $J$ = 7.6 Hz, 1 H), 7.70 (t, $J$ = 7.6 Hz, 1 H), 7.55–7.20 (m, 7 H), 6.70 (d, $J$ = 4.0 Hz, 1 H), 6.59 (t, $J$ = 5.7 Hz, 1 H), 6.37 (d, $J$ = 4.0 Hz, 1 H), 4.59 (d, $J$ = 5.7 Hz, 2 H), 3.85 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 162.3, 139.0, 136.2, 135.4, 133.9, 132.9, 131.7, 129.1, 128.8, 128.4, 128.1, 127.8, 118.5, 113.7, 112.1, 111.0, 43.7, 34.8 ppm. $C_{20}H_{17}N_3O$ (315.37): calcd. C 76.17, H 5.43; found C 76.27, H 5.57.

**1-Methyl-5-pyridin-4-ylpyrrole-2-carboxylic Acid Benzylamide (50):** 4-Bromopyridine hydrochloride (0.194 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **50** in 78% (0.227 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.58 (d, $J$ = 4.9 Hz, 2 H), 7.40–7.20 (m, 7 H), 6.90–6.80 (m, 1 H), 6.62 (d, $J$ = 3.7 Hz, 1 H), 6.24 (d, $J$ = 3.7 Hz, 1 H), 4.55 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 161.8, 149.7, 140.2, 138.6, 136.7, 129.2, 128.7, 127.6, 127.4, 123.3, 112.1, 110.0, 43.3, 34.7 ppm. $C_{18}H_{17}N_3O$ (291.35): calcd. C 74.20, H 5.88; found C 74.27, H 6.07.

**1-Methyl-5-pyridin-3-ylpyrrole-2-carboxylic Acid Benzylamide (51):** 3-Bromopyridine (0.158 g, 1 mmol) and **43** (0.321 g, 1.5 mmol) afforded **51** in 74% (0.215 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.59 (s, 1 H), 8.53 (d, $J$ = 4.0 Hz, 1 H), 7.66 (d, $J$ = 7.7 Hz, 1 H), 7.40–7.00 (m, 6 H), 6.95–6.85 (m, 1 H), 6.71 (d, $J$ = 3.9 Hz, 1 H), 6.17 (d, $J$ = 3.9 Hz, 1 H), 4.55 (d, $J$ = 5.7 Hz, 2 H), 3.88 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 160.9, 148.7, 147.6, 137.7, 135.3, 135.1, 127.6, 127.3, 127.0, 126.5, 126.2, 122.2, 110.9, 108.1, 42.1, 33.3 ppm. $C_{18}H_{17}N_3O$ (291.35): calcd. C 74.20, H 5.88; found C 74.34, H 6.01.

**2-Methylfuran-3-carboxylic Acid Benzylamide (52):**[25] The reaction of 2-methyl-3-furoyl chloride (0.347 g, 2.4 mmol) and benzylamine (0.214 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **52** in 73% (0.314 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.40–7.20 (m, 5 H), 7.14 (d, $J$ = 2.1 Hz, 1 H), 6.60–6.50 (m, 1 H), 6.44 (d, $J$ = 2.1 Hz, 1 H), 4.56 (d, $J$ = 5.8 Hz, 2 H), 2.62 (s, 3 H) ppm.

**5-(4-Formylphenyl)-2-methylfuran-3-carboxylic Acid Benzylamide (53):** 4-Bromobenzaldehyde (0.185 g, 1 mmol) and **52** (0.323 g, 1.5 mmol) afforded **53** in 68% (0.217 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.91 (s, 1 H), 7.80 (d, $J$ = 8.4 Hz, 2 H), 7.62 (d, $J$ = 8.4 Hz, 2 H), 7.40–7.25 (m, 5 H), 6.88 (s, 1 H), 6.60–6.40 (m, 1 H), 4.68 (d, $J$ = 5.7 Hz, 2 H), 2.68 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 191.5, 163.3, 158.0, 150.2, 138.3, 135.3, 135.0, 130.3, 128.7, 127.8, 127.5, 123.7, 118.0, 106.5, 43.5, 13.8 ppm. $C_{20}H_{17}NO_3$ (319.35): calcd. C 75.22, H 5.37; found C 75.04, H 5.31.

**5-(4-Cyanophenyl)-2-methylfuran-3-carboxylic Acid Benzylamide (54):** 4-Bromobenzonitrile (0.182 g, 1 mmol) and **52** (0.323 g, 1.5 mmol) afforded **54** in 78% (0.247 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.64 (d, $J$ = 8.4 Hz, 2 H), 7.60 (d, $J$ = 8.4 Hz, 2 H), 7.40–7.25 (m, 5 H), 6.89 (s, 1 H), 6.60–6.40 (m, 1 H), 4.68 (d, $J$ = 5.7 Hz, 2 H), 2.68 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 163.1, 158.1, 149.6, 138.2, 133.8, 132.6, 128.8, 127.8, 127.6, 123.7, 118.8, 118.0, 110.6, 106.5, 43.5, 13.8 ppm. $C_{20}H_{16}N_2O_2$ (316.35): calcd. C 75.93, H 5.10; found C 75.89, H 4.98.

**Methyl 4-(4-Benzylcarbamoyl-5-methylfuran-2-yl)benzoate (55):** Methyl 4-bromobenzoate (0.215 g, 1 mmol) and **52** (0.323 g, 1.5 mmol) afforded **55** in 67% (0.234 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.05 (d, $J$ = 8.4 Hz, 2 H), 7.64 (d, $J$ = 8.4 Hz, 2 H), 7.40–7.25 (m, 5 H), 6.84 (s, 1 H), 6.50–6.30 (m, 1 H), 4.61 (d, $J$ = 5.7 Hz, 2 H), 3.91 (s, 3 H), 2.70 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 166.7, 163.4, 157.6, 150.6, 138.3, 133.9, 130.1, 128.8, 128.7, 127.8, 127.6, 123.2, 117.8, 105.5, 52.1, 43.5, 13.8 ppm. $C_{21}H_{19}NO_4$ (349.38): calcd. C 72.19, H 5.48; found C 72.31, H 5.57.

**5-(4-Fluorophenyl)-2-methylfuran-3-carboxylic Acid Benzylamide (56):** 4-Bromofluorobenzene (0.175 g, 1 mmol) and **52** (0.323 g, 1.5 mmol) afforded **56** in 71% (0.219 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.62 (dd, $J$ = 8.4, 5.2 Hz, 2 H), 7.40–7.25 (m, 5 H), 7.14 (t, $J$ = 8.4 Hz, 2 H), 6.55 (s, 1 H), 6.20–6.00 (m, 1 H), 4.65 (d, $J$ = 5.7 Hz, 2 H), 2.70 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 163.6, 162.3 (d, $J$ = 247.5 Hz), 156.5, 150.9, 138.3, 128.8, 128.0, 127.6, 125.4 (d, $J$ = 8.0 Hz), 126.3 (d, $J$ = 3.2 Hz), 117.2, 115.8 (d, $J$ = 22.0 Hz), 102.8, 43.5, 13.7 ppm. $C_{19}H_{16}FNO_2$ (309.33): calcd. C 73.77, H 5.21; found C 73.64, H 5.21.

**2-Methyl-5-(3-nitrophenyl)furan-3-carboxylic Acid Benzylamide (57):** 3-Bromonitrobenzene (0.202 g, 1 mmol) and **52** (0.323 g, 1.5 mmol) afforded **57** in 72% (0.242 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.39 (s, 1 H), 8.06 (d, $J$ = 8.1 Hz, 1 H), 7.88 (d, $J$ = 8.1 Hz, 1 H), 7.52 (t, $J$ = 8.0 Hz, 1 H), 7.40–7.25 (m, 5 H), 6.92 (s, 1 H), 6.60–6.50 (m, 1 H), 4.60 (d, $J$ = 5.7 Hz, 2 H), 2.70 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 163.3, 157.7, 149.1, 148.7, 138.3, 131.5, 129.8, 128.9, 128.7, 127.8, 127.5, 121.9, 118.3, 117.9, 105.7, 43.5, 13.8 ppm. $C_{19}H_{16}N_2O_4$ (336.34): calcd. C 67.85, H 4.79; found C 67.69, H 4.89.

**5-(2-Cyanophenyl)-2-methylfuran-3-carboxylic Acid Benzylamide (58):** 2-Bromobenzonitrile (0.182 g, 1 mmol), **52** (0.323 g, 1.5 mmol) afforded **58** in 85% (0.269 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.87 (d, $J$ = 8.2 Hz, 1 H), 7.70–7.55 (m, 2 H), 7.40–7.25 (m, 7 H), 6.60–6.50 (m, 1 H), 4.60 (d, $J$ = 5.7 Hz, 2 H), 2.72 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 162.2, 157.1, 146.1, 137.4, 133.1, 132.0, 131.3, 127.6, 126.7, 126.3, 126.2, 124.6, 117.9, 116.8, 107.4, 105.2, 42.3, 12.7 ppm. $C_{20}H_{16}N_2O_2$ (316.35): calcd. C 75.93, H 5.10; found C 75.98, H 4.95.

**2-Methyl-5-pyridin-3-ylfuran-3-carboxylic Acid Benzylamide (59):** 3-Bromopyridine (0.158 g, 1 mmol) and **52** (0.323 g, 1.5 mmol) afforded **59** in 78% (0.228 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.70 (s, 1 H), 8.35–8.30 (m, 1 H), 7.77 (d, $J$ = 7.9 Hz, 1 H), 7.40–7.00 (m, 7 H), 6.92 (s, 1 H), 4.51 (d, $J$ = 5.7 Hz, 2 H), 2.61 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 163.2, 157.1, 147.8, 147.5, 144.3, 138.1, 130.2, 128.1, 127.7, 126.8, 125.8, 124.0, 117.3, 104.8, 42.9, 13.3 ppm. $C_{18}H_{16}N_2O_2$ (292.33): calcd. C 73.95, H 5.52; found C 74.07, H 5.41.

**1-Ethyl-3-methylpyrazole-5-carboxylic Acid Benzylamide (63):** The reaction of 1-ethyl-3-methylpyrazole-5-carbonyl chloride (0.413 g, 2.4 mmol) and benzylamine (0.214 g, 2 mmol) in triethylamine (4 mL) and dichloromethane (30 mL) at room temperature over 3 h gave **63** in 70% (0.340 g) yield after addition of an $H_2O$/HCl solution, extraction with dichloromethane, drying ($MgSO_4$), and purification by silica gel column chromatography. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.30–7.20 (m, 6 H), 6.29 (s, 1 H), 4.50–4.40 (m, 4 H), 2.15 (s, 3 H), 1.33 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 160.1, 146.7, 138.0, 135.1, 128.6, 127.5, 127.4, 106.2, 46.2, 43.2, 16.0, 13.2 ppm. $C_{14}H_{17}N_3O$ (243.30): calcd. C 69.11, H 7.04; found C 68.89, H 7.14.

**4-(4-Cyanophenyl)-1-ethyl-3-methylpyrazole-5-carboxylic Acid Benzylamide (64):** 4-Bromobenzonitrile (0.182 g, 1 mmol) and **63** (0.365 g, 1.5 mmol) afforded **64** in 78% (0.268 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.47 (d, $J$ = 8.4 Hz, 2 H), 7.30–7.10 (m, 5 H), 7.05–6.90 (m, 2 H), 5.75 (m, 1 H), 4.42 (q, $J$ = 7.5 Hz, 2 H), 4.38 (d, $J$ = 6.2 Hz, 2 H), 2.17 (s, 3 H), 1.44 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.8, 144.1, 136.2, 135.8, 132.8, 131.4, 129.3, 127.7, 126.9, 126.8, 117.9, 117.4, 109.9, 45.3, 42.7, 15.0, 11.1 ppm. $C_{21}H_{20}N_4O$ (344.41): calcd. C 73.23, H 5.85; found C 73.42, H 5.74.

**4-(4-Formylphenyl)-1-ethyl-3-methylpyrazole-5-carboxylic Acid Benzylamide (65):** 4-Bromobenzaldehyde (0.185 g, 1 mmol) and **63** (0. 365 g, 1.5 mmol) afforded **65** in 76% (0.264 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 9.93 (s, 1 H), 7.74 (d, $J$ = 8.4 Hz, 2 H), 7.35 (d, $J$ = 8.4 Hz, 2 H), 7.25–7.15 (m, 3 H), 7.00–6.90 (m, 2 H), 5.83 (m, 1 H), 4.46 (q, $J$ = 7.5 Hz, 2 H), 4.36 (d, $J$ = 6.2 Hz, 2 H),

2.17 (s, 3 H), 1.46 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 191.5, 159.9, 145.3, 138.7, 136.8, 135.1, 133.6, 130.3, 130.0, 128.7, 127.8, 127.7, 119.5, 46.4, 43.7, 16.0, 12.1 ppm. $C_{21}H_{21}N_3O_2$ (347.41): calcd. C 72.60, H 6.09; found C 72.51, H 6.01.

**1-Ethyl-3-methyl-4-(3-nitrophenyl)pyrazole-5-carboxylic Acid Benzylamide (66):** 3-Bromonitrobenzene (0.202 g, 1 mmol) and **63** (0. 365 g, 1.5 mmol) afforded **66** in 82% (0.299 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.05 (m, 2 H), 7.50 (d, $J$ = 8.2 Hz, 1 H), 7.44 (t, $J$ = 7.6 Hz, 1 H), 7.25–7.15 (m, 3 H), 7.05–6.95 (m, 2 H), 5.79 (m, 1 H), 4.37 (q, $J$ = 7.5 Hz, 2 H), 4.35 (d, $J$ = 6.2 Hz, 2 H), 2.17 (s, 3 H), 1.45 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 159.8, 148.3, 145.3, 136.8, 135.8, 134.1, 133.7, 129.7, 128.7, 127.7, 127.6, 124.3, 122.2, 118.3, 46.4, 43.7, 16.0, 12.0 ppm. $C_{20}H_{20}N_4O_3$ (364.40): calcd. C 65.92, H 5.53; found C 65.87, H 5.41.

**1-Ethyl-3-methyl-4-(3-trifluoromethylphenyl)pyrazole-5-carboxylic Acid Benzylamide (67):** 3-(Trifluoromethyl)bromobenzene (0.225 g, 1 mmol) and **63** (0. 365 g, 1.5 mmol) afforded **67** in 71% (0.275 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.60–7.20 (m, 7 H), 7.05–6.95 (m, 2 H), 5.60 (m, 1 H), 4.59 (q, $J$ = 7.5 Hz, 2 H), 4.38 (d, $J$ = 6.2 Hz, 2 H), 2.18 (s, 3 H), 1.46 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 160.3, 145.8, 137.2, 133.7, 133.4, 131.8 (q, $J$ = 32.5 Hz), 129.9, 129.1, 128.1, 127.9, 126.9 (q, $J$ = 3.7 Hz), 125.0 (q, $J$ = 272.0 Hz), 124.8 (q, $J$ = 3.8 Hz), 119.7, 106.0, 47.0, 44.1, 16.5, 12.4 ppm. $C_{21}H_{20}F_3N_3O$ (387.40): calcd. C 65.11, H 5.20; found C 65.19, H 5.01.

**4-(2-Cyanophenyl)-1-ethyl-3-methylpyrazole-5-carboxylic Acid Benzylamide (68):** 2-Bromobenzonitrile (0.182 g, 1 mmol) and **63** (0. 365 g, 1.5 mmol) afforded **68** in 80% (0.275 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.63 (d, $J$ = 8.2 Hz, 1 H), 7.50 (t, $J$ = 7.6 Hz, 1 H), 7.45–7.15 (m, 5 H), 7.00–6.95 (m, 2 H), 5.66 (m, 1 H), 4.55–4.35 (m, 4 H), 2.14 (s, 3 H), 1.48 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 158.4, 144.8, 135.9, 135.2, 132.9, 132.3, 132.0, 130.8, 127.6, 127.2, 126.6, 126.5, 116.6, 116.0, 112.7, 45.6, 42.6, 15.0, 11.0 ppm. $C_{21}H_{20}N_4O$ (344.41): calcd. C 73.23, H 5.85; found C 73.40, H 5.97.

**1-Ethyl-3-methyl-4-pyridin-3-ylpyrazole-5-carboxylic Acid Benzylamide (69):** 3-Bromopyridine (0.158 g, 1 mmol) and **63** (0. 365 g, 1.5 mmol) afforded **69** in 74% (0.237 g) yield. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 8.50–8.00 (m, 2 H), 7.45 (d, $J$ = 7.3 Hz, 1 H), 7.30–7.00 (m, 6 H), 6.00 (m, 1 H), 4.45 (q, $J$ = 7.5 Hz, 2 H), 4.41 (d, $J$ = 6.2 Hz, 2 H), 2.19 (s, 3 H), 1.46 (t, $J$ = 7.5 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 159.2, 148.8, 146.9, 144.3, 136.3, 133.2, 127.6, 126.8, 126.6, 122.5, 115.7, 45.3, 42.7, 15.0, 11.1 ppm. $C_{19}H_{20}N_4O$ (320.39): calcd. C 71.23, H 6.29; found C 70.47, H 6.18.

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