Synthesis X.-F. Wu et al. Paper

Palladium-Catalyzed Carbonylative Synthesis of *N*-Benzoylindoles with $Mo(CO)_6$ as the Carbon Monoxide Source

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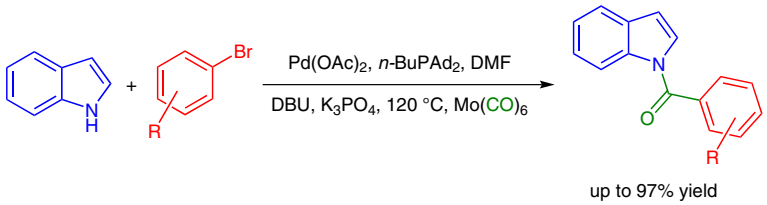

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Abstract A mild and carbon monoxide gas-free palladium-catalyzed aminocarbonylation of indole has been developed for the synthesis of *N*-benzoylindoles. This method uses $Mo(CO)_6$ as a convenient CO-precursor and $BuPAd_2$ as the ligand. A number of substituents on the aryl bromide species is tolerated under the presented conditions and gave the desired products in up to excellent yields.

Key words benzoylindole, aminocarbonylation, palladium catalyst, molybdenum hexacarbonyl, indole

As an omnipresent structure, indole plays a superior role in material science and in the chemistry of pharmaceuticals, agrochemicals, flavoring agents, and dyes.[1] One of the most important pharmacological actions of indole derivatives is their application to CNS disorders, for example, reserpine (**4**),[2] or their use as anti-inflammatory properties, for example, indometacin (**1**, Figure 1).[3] Some other indole containing structures show cytostatic effect, such as vobasidin A (**2**),[4] or act as nonpeptide angiotensin II receptor antagonist for the treatment of hypertension, for example, **3**.[5]

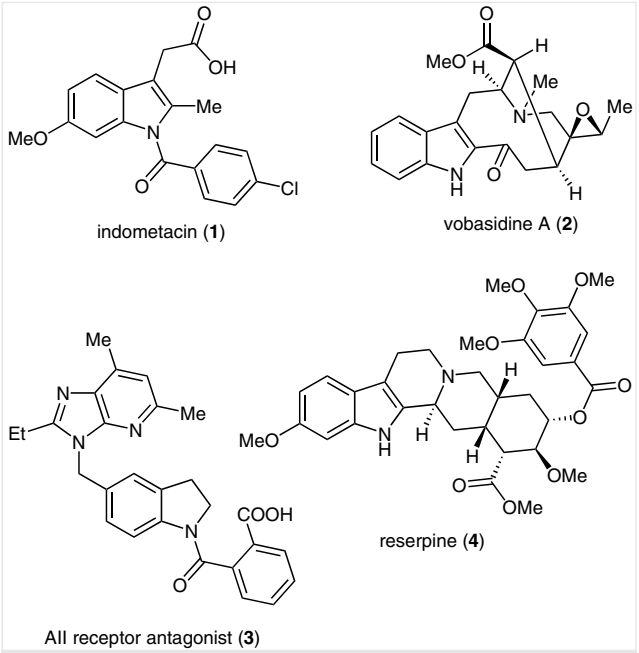


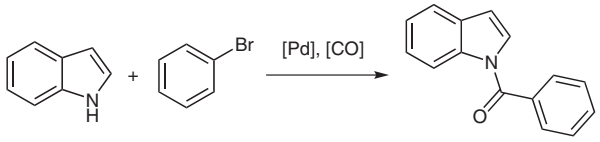
Figure 1 Selected pharmacologically relevant indoles

Due to the versatile applications of 2,3-benzopyrrole containing structures, many efforts have been made towards the synthesis or direct functionalization of these compounds.[6] Among the extensive achievements, selected examples for the direct N-functionalization are mentioned here. Notably, the NH group is not the most reactive center for electrophilic reactions, which is C3, and usually has to be transformed preliminary into the indolyl anion. Due to the weak NH acidity [pK, e.g., 16.97 (H_2O)[7] and 21.0 (DMSO)[8]], the Mitsunobu reaction requires additional electron-withdrawing substituents on the indole-system to access more branched *N*-alkyl derivatives.[9] Many other protocols for the N-alkylation and N-arylation have been developed such as the Morita–Baylis–Hilman reaction[10] or copper-[11] and palladium[12]-catalyzed N-arylations, to name only a few. Additionally, several procedures for the direct N-benzoylation of indole have been reported in the literature. The use of benzoyl chloride[13] has been taken as a standard procedure to obtain *N*-benzoylindoles. Palladium-catalyzed carbonylation reaction has been explored in benzoylindoles synthesis as well. Notably, Quesnel and Arndtsen reported on the Pd-catalyzed in situ generation of the acid chloride from iodobenzene under the use of 1 atm of CO gas, leading to 85% benzoylindole.[14] Additionally, the group of Bremner

reported in 2004 on the reaction of carboxylic acids with indole, with DMAP and DCC as the activating agents.[15] In 2010, Ren and Yamane published a protocol using $Mo(CO)_6$ as CO-source and catalyst for the carbonylation of aryl iodides, and one example on iodobenzene and indole to give 60% benzoylindole was given.[16]

Transition-metal-catalyzed carbonylation is a powerful and versatile tool to access a broad variety of carbonyl compounds.[17] Since the first reported Pd-catalyzed aminocarbonylation in 1974,[18] extensive work in the field of carbonylation chemistry led to the development of a wide range of catalytic systems that allow for the synthesis of various carbonyl-containing compounds.[19] Many efforts have been made to replace gaseous carbon monoxide as C1-building block by easier to handle carbonyl sources. For instance, the group of Skrydstrup developed COgen (9-methylfluorene-9-carbonyl chloride) as a convenient organic CO-precursor that also allows for the introduction of ^{13}C-labeled carbonyl groups.[20] Additionally, transition metal carbonyls such as $Mo(CO)_6$ have been proven as beneficial CO-source in a variety of carbonylative coupling reactions. The group of Larhed reported on the broad applicability of the metal carbonyls.[21] Recently, we showed that the molybdenum CO-precursor is also appropriate for the tandem dicarbonylative coupling of *o*-dibromobenzenes to obtain phthalimides.[22] Here, we report our recent results on the palladium-catalyzed carbonylative synthesis of benzoylindoles with $Mo(CO)_6$ as the CO source.

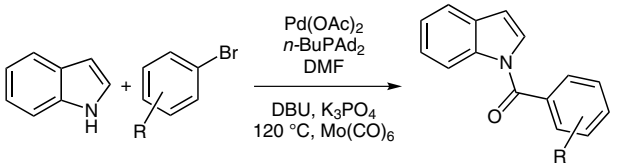
Table 1 Optimization of the Synthesis of *N*-Benzoylindole[a]



Entry	Ligand	CO source	Yield (%)[b]
1[c]	*n*-BuPAd$_2$	$Mo(CO)_6$	0
2	*n*-BuPAd$_2$	$Mo(CO)_6$	90
3	Ph_3P	$Mo(CO)_6$	0
4	Cy_3P	$Mo(CO)_6$	0
5	dppp	$Mo(CO)_6$	0
6[d]	*n*-BuPAd$_2$	$Mo(CO)_6$	0
7	*n*-BuPAd$_2$	$Co_2(CO)_8$	85
8	*n*-BuPAd$_2$	$W(CO)_6$	68
9	*n*-BuPAd$_2$	$Cr(CO)_6$	95

[a] Reaction conditions: indole (0.5 mmol), bromobenzene (0.5 mmol), DBU (0.5 mmol), K_3PO_4 (0.5 mmol), CO source (0.5 mmol), $Pd(OAc)_2$ (3 mol%), ligand (6 mol%), DMF (3 mL), argon atmosphere, 120 °C, 16 h.
[b] GC yields with hexadecane as internal standard.
[c] Reaction was carried out without K_3PO_4.
[d] Reaction was carried out without DBU.

Table 2 Palladium-Catalyzed Carbonylative Synthesis of *N*-Benzoylindoles[a]



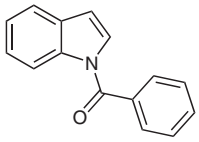
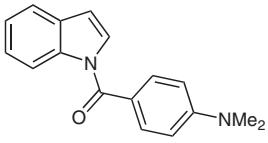
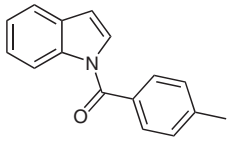
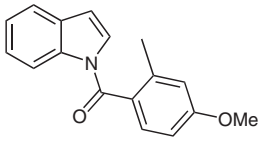
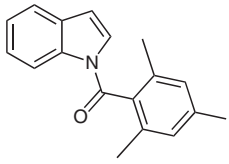
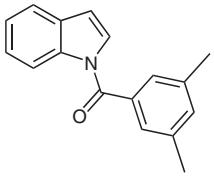
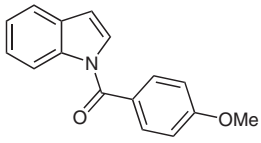
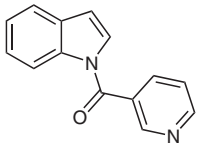
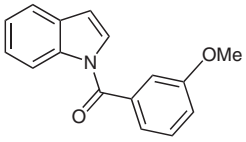
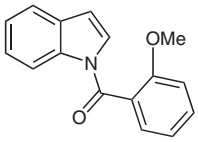
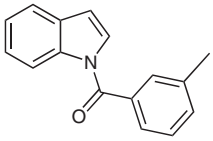
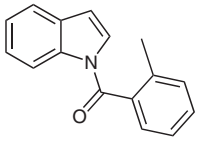
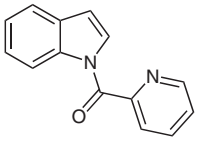
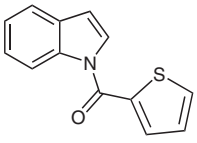
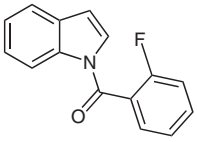
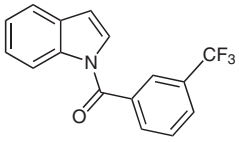
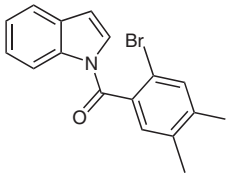
Entry	Product	Yield (%)[b]
1		89
2		53
3		97
4		98
5		42
6		80
7		94
8		50

Table 2 (continued)

Entry	Product	Yield (%)[b]
9		38
10		87
11		23
12		23
13		28
14		39
15		25
16		49
17		18

[a] Reaction conditions: indole (0.5 mmol), aryl bromide (0.5 mmol), DBU (0.5 mmol), K_3PO_4 (0.5 mmol), $Mo(CO)_6$ (0.5 mmol), $Pd(OAc)_2$ (3 mol%), *n*-$BuPAd_2$ (6 mol%), DMF (3 mL), argon atmosphere, 120 °C, 16 h.
[b] Isolated yields.

Initial experiments for the carbonylative coupling of indole and bromobenzene were carried out using $Pd(OAc)_2$ as the palladium source and $BuPAd_2$ as the ligand (Table 1, entry 1). Our experience in the field of carbonylative C–N coupling showed that the CataCXium® A [di(1-adamantyl)-*n*-butylphosphine] ligand, developed by Beller et al., proved to be excellent for aminocarbonylations.[23] DBU was used as the base of choice due to its ability to coordinate at the molybdenum to promote the in situ release of CO.[24] Unfortunately, no desired product could be detected in the first testing. To our delight, when performing the reaction with the addition of one equivalent of K_3PO_4 as the base, 90% yield of benzoylindole was formed (Table 1, entry 2). Then, investigation on the influence of different ligands on this reaction was carried out. Interestingly, standard ligands such as Ph_3P (Table 1, entry 3) and the bidentate dppp did not show any conversion of the substrate.

Notably, when performing the reaction only with K_3PO_4 and without the addition of DBU no reaction took place. Afterwards, different metal carbonyls were tested as CO sources. According to our previous work,[22] $Cr(CO)_6$ (Table 1, entry 9) shows high potential as CO-precursor. Cobalt and tungsten carbonyls lead to lower yields. Chromium carbonyl gave better yield, however, due to the high toxicity of chromium salts $Mo(CO)_6$ was used for further studies.

With a working procedure in hand, substrate testing was started. As shown in Table 2, the presented method shows high yields up to 98% for electron-donating substituents such as methyl (Table 2, entries 3, 6) or methoxy (Table 2, entries 4, 7, and 10). The lower yields of the reaction with mesityl bromide (Table 2, entry 5) can be explained by the steric hindrance due to the two *ortho* methyl groups. A methoxy group attached in *meta* position (Table 2, entry 9) decreases the yield to 38%. This may cohere with the loss of the electron donation and the *I*-effect. The developed procedure works also for electron-withdrawing substituents. Heterocyclic bromides such as pyridyl and thiophenyl can also be applied as substrates for this transformation, although the yields are lower compared to the model reaction.[25]

In summary, a versatile method to obtain various *N*-benzoylindoles via palladium-catalyzed aminocarbonylation of aryl bromides has been elaborated. $Mo(CO)_6$ was used as a convenient and easy-to-handle carbonyl source. The protocol works very well for electron-donating substituents such as methyl and methoxy, and also applicable for heterocyclic arenes.

Distilled H_2O was used as solvent. All commercially available chemicals were used without further purification. NMR spectra were recorded on Bruker ARX 300 and Bruker ARX 400 spectrometers. ^1H and ^{13}C spectra were referenced to the residual solvent signals in the deuterated solvent. Standard abbreviations were used to denote the multiplicity of the signals. Gas chromatography/mass analysis was

carried out using an Agilent HP-5890 with Agilent HP-5973 Mass Selective Detector (EI) and an HP-5 capillary column using He as carrier gas. Column chromatography was performed using Merck silica Gel 60 (0.043–0.06 mm) and distilled solvents were used.

N-Benzoylindole; Typical Procedure

An argon flushed pressure tube was charged with indole (59 mg, 0.5 mmol), bromobenzene (62 μL, 0.5 mmol), $Mo(CO)_6$ (132 mg, 0.5 mmol), DBU (75 μL, 0.5 mmol), K_3PO_4 (106 mg, 0.5 mmol), $Pd(OAc)_2$ (3.4 mg, 3 mol%), $BuPAd_2$ (10.8 mg, 6 mol%), and DMF (3 mL). The tube was subsequently sealed and the mixture was stirred at 120 °C for 16 h. Afterwards, the reaction mixture was diluted with CH_2Cl_2 (3 × 5 mL) and washed with H_2O (3 × 5 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), the combined organic phases were dried (Na_2SO_4), and the solvent was evaporated. The crude product was purified by column chromatography (pentane–EtOAc (8:2) with addition of 0.5% Et_3N) to give benzoylindole as a viscous oil that solidified on standing; yield: 98 mg (89%); mp 64–65 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.42 (1 H, d, ^3J = 8.0 Hz, CH-7), 7.80–7.69 (2 H, m, CH-10 + 14), 7.66–7.58 (2 H, m, CH-12 + 4), 7.53 (2 H, dd, ^3J = 8.1 Hz, ^4J = 6.3 Hz, CH-11 + 13), 7.45–7.28 (3 H, m, CH-2 + 5 + 6), 6.62 (1 H, d, ^3J = 3.7 Hz, CH-3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 168.8 (C=O), 136.2 (C_q-7a), 134.7 (C_q-9), 132.0 (CH-12), 130.9 (C_q-3a), 129.3 (CH-10 + 14), 128.7 (CH-11 + 13), 127.7 (CH-4), 125.0 (CH-2), 124.1 (CH-5), 121.0 (CH-6), 116.5 (CH-7), 108.7 (CH-3).

GC/MS (EI 70 eV): *m*/*z* (%) = 221 ([M]$^+$, 37), 116 (11), 105 (100), 89 (18), 77 (68), 63 (15), 51 (24), 50 (11).

N-(4-Dimethylaminobenzoyl)indole

Yield: 70 mg (53%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.31 (1 H, ddd, ^3J = 8.1 Hz, ^4J = 1.2 Hz, ^5J = 0.6 Hz, CH-7), 7.76–7.69 (2 H, m, CH-10 + 14), 7.64–7.59 (1 H, m, CH-4), 7.47 (1 H, d, ^3J = 3.7 Hz, CH-6), 7.40–7.25 (2 H, m, CH-2 + 5), 6.77–6.69 (2 H, m, CH-11 + 13), 6.61 (1 H, d, ^3J = 3.7 Hz, CH-3), 3.08 (6 H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.7 (C=O), 153.0 (C_q-12), 136.3 (C_q-7a), 132.2 (CH-10 + 14), 130.7 (C_q-3a), 128.2 (CH-4), 124.4 (CH-2), 123.2 (CH-5), 120.8 (CH-6), 120.6 (C_q-9), 116.1 (CH-7), 111.0 (CH-11 + 13), 107.2 (CH-3), 40.2 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 264 ([M]$^+$, 17), 149 (13), 148 (100), 116 (13), 104 (10), 89 (18), 77 (14).

N-(4-Methylbenzoyl)indole

Yield: 114 mg (97%); white solid; mp 87–89 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.44–8.33 (1 H, m, CH-7), 7.65 (2 H, d, ^3J = 8.1 Hz, CH-10 + 14), 7.43–7.28 (5 H, m, CH-2 + 5 + 6 + 11 + 13), 7.13 (1 H, dd, ^3J = 8.6 Hz, ^4J = 2.5 Hz, CH-4), 6.61 (1 H, dd, ^3J = 3.7 Hz, ^5J = 0.8 Hz, CH-3), 1.43 (3 H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.9 (C=O), 142.7 (C_q-9), 136.2 (C_q-7a), 131.8 (C_q-12), 130.9 (C_q-3a), 129.5 (CH-10 + 14), 129.4 (CH-11 + 13), 127.8 (CH-4), 124.9 (CH-2), 123.9 (CH-5), 121.0 (CH-6), 116.5 (CH-7), 108.4 (CH-3), 21.8.

GC/MS (EI 70 eV): *m*/*z* (%) = 235 ([M]$^+$, 28), 119 (100), 116 (15), 91 (49), 90 (10), 89 (31), 65 (26), 63 (24), 39 (12).

N-(4-Methoxy-2-methylbenzoyl)indole

Yield: 135 mg (98%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.33 (1 H, dd, ^3J = 8.2 Hz, ^4J = 1.1 Hz, CH-7), 7.60 (1 H, ddd, ^3J = 7.4 Hz, ^4J = 1.6 Hz, ^5J = 0.7 Hz, CH-4), 7.43–7.27 (2 H, m, CH-5 + 6), 7.13 (1 H, d, ^3J = 3.8 Hz, CH-2), 6.88–6.77 (3 H, m, CH-11 + 13 + 14), 6.59 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3), 3.87 (3 H, s, OCH_3), 2.36 (3 H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1 (C=O), 161.3 (COMe), 138.9 (CH-14), 135.8 (C_q-7a), 132.9 (C_q-9), 131.1 (C_q-3a), 130.0 (CH-11), 127.4 (CH-4), 125.0 (CH-2), 124.0 (CH-5), 121.0 (CH-6), 116.5 (CH-7), 113.0 (CH-13), 111.1 (C_q-10), 108.7 (CH-3), 55.5 (OCH_3), 19.9 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 265 ([M]$^+$, 17), 150 (14), 149 (100), 121 (13), 91 (12).

N-(2,4,6-Trimethylbenzoyl)indole

Yield: 55 mg (42%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.69 (1 H, dd, ^3J = 8.2 Hz, ^4J = 1.0 Hz, CH-7), 7.59 (1 H, ddd, ^3J = 7.7 Hz, ^4J = 1.4 Hz, ^5J = 0.7 Hz, CH-4), 7.43 (1 H, ddd, ^3J = 8.4 Hz, ^3J = 7.3 Hz, ^4J = 1.4 Hz, CH-6), 7.38–7.30 (1 H, m, CH-5), 6.93 (2 H, d, ^4J = 1.3 Hz, ^4J = 0.8 Hz, CH-11 + 13), 6.81 (1 H, d, ^3J = 3.8 Hz, CH-2), 6.54 (1 H, d, ^3J = 3.8 Hz, CH-3), 2.35 (3 H, s, CH_3), 2.19 (6 H, d, ^4J = 0.7 Hz, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.1 (C=O), 139.7 (C_q-9), 134.7 (C_q-7a), 131.2 (C_q-10 + 14), 129.7 (C_q-3a), 128.5 (CH-13 + 11), 126.6 (CH-4), 125.3 (CH-2), 124.3 (CH-5), 123.8 (C_q-12), 121.0 (CH-6), 116.9 (CH-7), 109.4 (CH-3), 21.4 (CH_3), 19.3 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 263 ([M]$^+$, 12), 148 (11), 147 (100), 119 (18), 91 (10).

N-(3,5-Dimethylbenzoyl)indole

Yield: 100 mg (80%); light yellow solid; mp 79–81 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.43–8.37 (1 H, m, CH-7), 7.61 (1 H, ddd, ^3J = 7.6 Hz, ^4J = 1.5 Hz, ^5J = 0.8 Hz, CH-4), 7.42–7.27 (5 H, m, CH-2 + 5 + 6 + 10 + 14), 7.27–7.20 (1 H, m, CH-12), 6.60 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3), 2.44–2.36 (6 H, m, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3 (C=O), 138.5 (C_q-10 + 14), 136.2 (C_q-7a), 134.7 (C_q-9), 133.6 (CH-12), 130.9 (C_q-3a), 127.9 (CH-4), 126.9 (CH-11 + 13), 125.0 (CH-2), 124.0 (CH-5), 121.0 (CH-6), 116.6 (CH-7), 108.4 (CH-3), 21.4 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 249 ([M]$^+$, 26), 134 (10), 133 (100), 105 (28), 79 (11), 77 (12).

N-(4-Methoxybenzoyl)indole

Yield: 118 mg (94%); light yellow solid; mp 137–138 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.39–8.31 (1 H, m, CH-7), 7.79–7.71 (2 H, m, CH-10 + 14), 7.61 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^5J = 0.7 Hz, CH-4), 7.43–7.27 (3 H, m, CH-2 + 5 + 6), 7.06–6.98 (2 H, m, CH-11 + 13), 6.62 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3), 3.91 (3 H, s, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.4 (C=O), 162.8 (COMe), 136.2 (C_q-7a), 131.8 (CH-10 + 14), 130.8 (C_q-3a), 127.9 (CH-4), 126.7 (C_q-9), 124.8 (CH-2), 123.8 (CH-5), 121.0 (CH-6), 116.3 (CH-7), 114.0 (CH-11 + 13), 108.1 (CH-3), 55.7 (OCH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 251 ([M]$^+$, 17), 135 (100), 116 (23), 107 (11), 92 (27), 89 (25), 77 (27), 64 (16), 63 (25).

(1*H*-Indol-1-yl)(pyridin-3-yl)methanone

Yield: 55.5 mg (50%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.00–8.96 (1 H, m, CH-10), 8.84 (1 H, dd, ^4J = 4.9 Hz, ^5J = 1.7 Hz, CH-12), 8.41 (1 H, d, ^3J = 8.1 Hz, CH-7), 8.06 (1 H, ddd, ^3J = 7.9 Hz, ^4J = 2.3 Hz, ^4J = 1.7 Hz, CH-14), 7.61 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^5J = 0.7 Hz, CH-4), 7.49 (1 H, ddd, ^3J = 7.9 Hz, ^3J = 4.9 Hz, ^4J = 0.9 Hz, CH-13), 7.45–7.30 (2 H, m, CH-6 + 5), 7.22 (1 H, d, ^3J = 3.8 Hz, CH-2), 6.67 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.4 (C=O), 152.5 (C_q-9), 149.7 (CH-10), 136.8 (CH-12), 136.0 (C_q-7a), 130.9 (C_q-3a), 130.8 (CH-14), 126.9 (CH-4), 125.4 (CH-2), 124.5 (CH-5), 123.6 (CH-13), 121.2 (CH-6), 116.5 (CH-7), 109.8 (CH-3).

GC/MS (EI 70 eV): *m*/*z* (%) = 222 ([M]$^+$, 54), 116 (25), 106 (100), 89 (37), 78 (84), 63 (24), 62 (10), 51 (47), 50 (25), 39 (13).

N-(3-Methoxybenzoyl)indole

Yield: 48 mg (38%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.46 (1 H, d, ^3J = 8.6 Hz, CH-7), 7.58 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^5J = 0.7 Hz, CH-11), 7.51 (1 H, ddd, ^3J = 8.4 Hz, ^4J = 7.4 Hz, ^5J = 1.8 Hz, CH-6), 7.45 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.8 Hz, ^5J = 0.4 Hz, CH-4), 7.42–7.35 (1 H, m, CH-2), 7.31 (1 H, ddd, ^3J = 7.4 Hz, ^3J = 7.4 Hz, ^4J = 1.3 Hz, CH-5), 7.13–7.05 (2 H, m, CH-12 + 13), 7.03 (1 H, dd, ^3J = 8.4 Hz, ^4J = 0.9 Hz, CH-14), 6.56 (1 H, dd, ^3J = 3.8 Hz, ^4J = 0.8 Hz, CH-3), 3.78 (3 H, s, OCH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 168.6 (C=O), 159.8 (COMe), 136.1 (C_q-7a), 136.0 (C_q-9), 130.9 (C_q-3a), 129.8 (CH-13), 127.7 (CH-4), 125.1 (CH-2), 124.1 (CH-5), 121.5 (CH-14), 121.0 (CH-6), 118.16 (CH-12), 116.6 (CH-7), 114.2 (CH-10), 108.7 (CH-3), 55.65 (OCH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 251 ([M]$^+$, 20), 135 (100), 116 (19), 92 (27), 89 (23), 77 (33), 64 (12), 63 (22).

N-(2-Methoxybenzoyl)indole

Yield: 109 mg (87%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.46 (1 H, d, ^3J = 8.6 Hz, CH-7), 7.58 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^5J = 0.7 Hz, CH-11), 7.51 (1 H, ddd, ^3J = 8.4 Hz, ^3J = 7.4 Hz, ^4J = 1.8 Hz, CH-12), 7.45 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.8 Hz, ^5J = 0.4 Hz, CH-4), 7.42–7.35 (1 H, m, CH-6), 7.31–7.05 (3 H, m, CH-2 + 5 +13), 7.03 (1 H, dd, ^3J = 8.4 Hz, ^5J = 0.9 Hz, CH-14), 6.56 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3), 3.78 (3 H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.3 (C=O), 156.4 (C-OMe), 135.7 (C_q-7a), 132.2 (CH-12), 131.1 (C_q-3a), 129.1 (CH-13), 127.5 (CH-4), 124.9 (CH-2), 124.9 (C_q-9), 124.0 (CH-5), 120.9 (CH-14), 120.8 (CH-6), 116.6 (CH-7), 111.5 (CH-11), 108.7 (CH-3), 55.7 (OCH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 251 ([M]$^+$, 41), 135 (100), 116 (23), 107 (31), 92 (38), 89 (33), 77 (43), 76 (11), 64 (21), 63 (38), 50 (10).

N-(3-Methylbenzoyl)indole

Yield: 27 mg (23%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.45–8.35 (1 H, m, CH-7), 7.64–7.49 (5 H, m, CH-4 + 10 + 12 + 13 + 14), 7.46–7.28 (3 H, m, CH-2 + 5 + 6), 6.61 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3), 2.45 (3 H, s, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1 (C=O), 138.7 (C_q-11), 136.2 (C_q-7a), 134.7 (C_q-9), 132.8 (CH-12), 130.9 (C_q-3a), 129.8 (CH-10), 128.5 (CH-13), 127.8 (CH-4), 126.4 (CH-14), 125.0 (CH-2), 124.0 (CH-5), 121.0 (CH-6), 116.6 (CH-7), 108.6 (CH-3), 21.52 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 235 ([M]$^+$, 31), 119 (100), 91 (45), 89 (10), 65 (13).

N-(2-Methylbenzoyl)indole

Yield: 27 mg (23%); viscous liquid.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.39 (1 H, d, ^3J = 7.3 Hz, CH-7), 7.70–7.58 (3 H, m, CH-4 + 10 + 14), 7.45–7.27 (5 H, m, CH-2 + 5 + 6 + 11 + 13), 6.61 (1 H, dd, ^3J = 3.7 Hz, ^5J = 0.8 Hz, CH-3), 2.47 (3 H, s, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 168.9 (C=O), 142.7 (C_q-12), 136.2 (C_q-7a), 131.8 (C_q-9), 130.9 (C_q-3a), 129.5 (CH-10 + 14), 129.4 (CH-11 + 13), 127.8 (CH-4), 124.9 (CH-2), 123.9 (CH-5), 121.0 (CH-6), 116.5 (CH-7), 108.4 (CH-3), 21.8 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 235 ([M]$^+$, 29), 119 (100), 116 (13), 91 (58), 90 (10), 89 (29), 65 (29), 63 (24), 39 (15).

(1*H*-Indol-1-yl)(pyridin-2-yl)methanone

Yield: 31 mg (28%); light yellow solid; mp 65–67 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.75 (1 H, ddd, ^3J = 4.8 Hz, ^4J = 1.7 Hz, ^5J = 0.9 Hz, CH-11), 8.59–8.49 (1 H, m, CH-7), 8.09 (1 H, ddd, ^3J = 7.9 Hz, ^4J = 1.1 Hz, ^5J = 1 Hz, CH-14), 8.04–7.89 (2 H, m, CH-12 + 13), 7.60 (1 H, ddd, ^3J = 7.4 Hz, ^4J = 1.6 Hz, ^5J = 0.7 Hz, CH-4), 7.52 (1 H, ddd, ^3J = 7.6 Hz, ^4J = 4.8 Hz, ^5J = 1.3 Hz, CH-6), 7.45–7.27 (3 H, m, CH-2 + 5), 6.64 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.8 (C=O), 152.5 (C_q-9), 148.7 (CH-11), 137.5 (CH-11), 136.6 (C_q-7a), 130.9 (C_q-3a), 128.6 (CH-4), 126.3 (CH-12), 125.9 (CH-14), 125.1 (CH-2), 124.3 (CH-5), 121.0 (CH-6), 117.0 (CH-7), 109.3 (CH-3).

GC/MS (EI 70 eV): *m*/*z* (%) = 222 ([M]$^+$, 55), 221 (23), 106 (44), 89 (13), 78 (100), 51 (13).

(1*H*-Indol-1-yl)(thiophen-2-yl)methanone

Yield: 44 mg (39%); viscous liquid.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.41 (1 H, d, ^3J = 8.1 Hz, CH-7), 7.74–7.66 (3 H, m, CH-2 + 11 + 13), 7.62 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^5J = 0.8 Hz, CH-4), 7.45–7.27 (2 H, m, CH-5 + 6), 7.20 (1 H, dd, ^3J = 4.9 Hz, ^3J = 3.9 Hz, CH-12), 6.68 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 161.8 (C=O), 137.3 (C_q-9), 136.3 (C_q-7a), 133.46 (CH-13), 132.78 (CH-11), 130.8 (C_q-3a), 127.7 (CH-4), 127.17 (CH-12), 125.1 (CH-2), 124.1 (CH-5), 121.1 (CH-6), 116.4 (CH-7), 108.9 (CH-3).

GC/MS (EI 70 eV): *m*/*z* (%) = 227 ([M]$^+$, 32), 111 (100), 39 (10).

N-(2-Fluorobenzoyl)indole

Yield: 35 mg (25%); viscous liquid.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.48 (1 H, d, ^3J = 8.1 Hz, CH-7), 7.64–7.52 (3 H, m, CH-4 + 12 + 13), 7.45–7.37 (1 H, m, CH-6), 7.37–7.29 (2 H, m, CH-5 + 14), 7.24–7.19 (1 H, m, CH-11), 7.13 (1 H, dd, ^3J = 3.8 Hz, ^4J = 2.5 Hz, CH-2), 6.62 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.5 (C=O), 159.1 (d, ^1J = 252.0 Hz, CF), 135.8 (C_q-7a), 133.2 (d, ^3J = 8.1 Hz, CH-12), 131.1 (C_q-3a), 130.09 (d, ^3J = 2.7 Hz, CH-14), 126.9 (CH-4), 125.3 (CH-2), 124.74 (d, ^4J = 3.6 Hz, CH-13), 124.4 (CH-5), 123.52 (d, ^2J = 16.0 Hz, C_q-9), 121.1 (CH-6), 116.6 (CH-7), 116.5 (d, ^2J = 21.0 Hz, CH-11), 109.6 (CH-3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –112.72.

GC/MS (EI 70 eV): *m*/*z* (%) = 239 ([M]$^+$, 34), 123 (100), 95 (28).

N-(3-Trifluorobenzoyl)indole

Yield: 71 mg (49%); light yellow solid; mp 83–86 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.32 (1 H, d, ^3J = 8.1 Hz, CH-7), 7.94–7.92 (1 H, m, CH-11), 7.86–7.76 (2 H, m, CH-13 + 14), 7.63–7.56 (1 H, m, CH-4), 7.53 (1 H, ddd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, ^5J = 0.7 Hz, CH-12),

7.32 (1 H, ddd, ^3J = 8.3 Hz, ^4J = 7.8 Hz, ^5J = 1.4 Hz, CH-6), 7.28–7.22 (1 H, m, CH-5), 7.11 (1 H, d, ^3J = 3.8 Hz, CH-2), 6.57 (1 H, dd, ^3J = 3.8 Hz, ^5J = 0.8 Hz, CH-3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.2 (C=O), 136.1 (C_q-7a), 135.6 (CH-14), 132.4 (q, ^4J = 1.4 Hz, C_q-9), 131.49 (q, ^2J = 33.1 Hz, CH-11), 130.9 (C_q-3a), 129.4 (CH-13), 128.45 (q, ^3J = 3.6 Hz, CH-12), 127.0 (CH-4), 126.04 (q, ^3J = 3.8 Hz, CH-10), 125.4 (CH-2), 124.5 (CH-5), 121.2 (CH-6), 120.0 (q, ^1J = 272.7 Hz, CF_3), 116.6 (CH-7), 109.6 (CH-3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –62.81.

GC/MS (EI 70 eV): *m*/*z* (%) = 290 (15), 289 ([M]$^+$, 80), 174 (18), 173 (100), 145 (96), 95 (11), 89 (11).

(2-Bromo-4,5-dimethylphenyl)(1*H*-indol-1-yl)methanone

Yield: 30 mg (18%); light yellow solid; mp 64–67 °C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38 (1 H, d, ^3J = 8.1 Hz, CH-7), 7.65–7.50 (3 H, m, CH-4 + 11 + 14), 7.51–7.27 (2 H, m, CH-5 + 6), 7.01 (1 H, d, ^3J = 3.8 Hz, CH-2), 6.63–6.57 (1 H, m, CH-3), 2.33 (3 H, s, CH_3), 2.27 (3 H, s, CH_3).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 167.1 (C=O), 141.3 (C_q-10), 136.7 (C_q-7), 134.5 (C_q-9), 133.9, 130.0 (C_q-3a), 127.1 (CH-4), 125.3 (CH-2), 124.9, 124.3 (CH-5), 121.0 (CH-6), 120.9, 116.6 (CH-7), 116.49, 109.5 (CH-3), 19.8 (CH_3), 19.40 (CH_3).

GC/MS (EI 70 eV): *m*/*z* (%) = 329 ([M (^{81}Br)]$^+$, 20), 327 ([M (^{79}Br)]$^+$, 20), 213 (98), 211 (100), 104 (22), 103 (16), 77 (10).

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Supporting Information

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