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Palladium(0)-Catalyzed Carbonylative Synthesis of *N*-Acylsulfonamides via Regioselective Acylation

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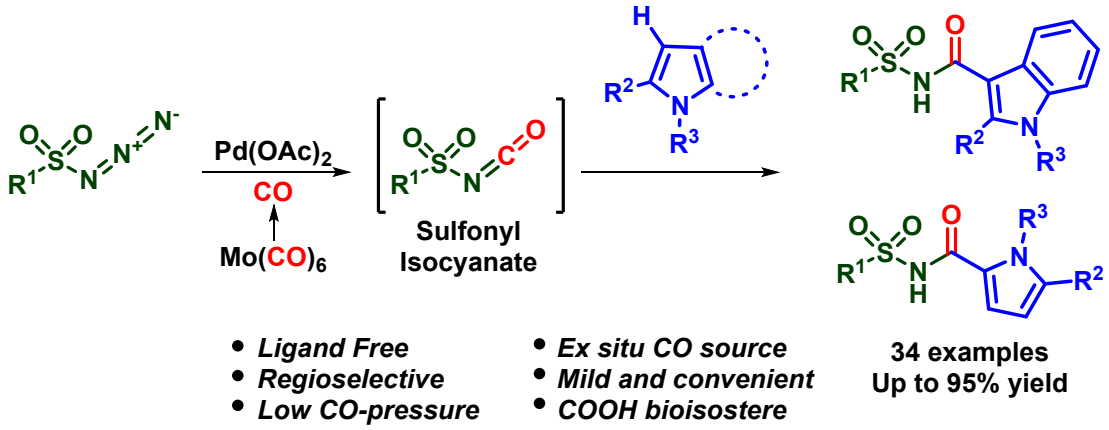
ABSTRACT

N-Acylsulfonamides represent an important bioisotere of carboxylic acids that allow for greater molecular elaboration and enhanced hydrogen bonding capabilities. Herein, we present a mild and convenient palladium(0)-catalyzed synthesis of *N*-acylsulfonamides via the carbonylative coupling of sulfonyl azides and electron-rich heterocycles. The reaction proceeds via *in situ* generation of a sulfonyl isocyanate followed by regioselective acylation of an indole or pyrrole nucleophile. This approach has been used to synthesize 34 indole and pyrrole-substituted *N*-acylsulfonamides in yields of up to 95%. Importantly, this process is ligand-free, compatible with an *ex situ* solid CO-source and requires only slightly elevated temperatures making it a highly attractive method for the preparation of this important class of compounds. This study further investigated the possibility of labelling *N*-acylsulfonamides with carbon-11 to facilitate biological evaluation and *in vivo* studies with positron emission tomography.

GRAPHICAL ABSTRACT



INTRODUCTION

N-Acylsulfonamides are a useful carboxylic acid bioisostere; they are hydrolytically and enzymatically stable,[1] and possess a similar pK_a range and greater hydrogen bonding capability compared to carboxylic acids. However, unlike carboxylic acids, they can be further elaborated to modulate both physicochemical[2] and biological properties.[3,4] Figure **1** shows this bioisostere is indeed already present in a variety of currently marketed drugs, drug candidates and pharmacological tools, in particular, the anti-Hepatitis C drugs beclabuvir,[5] asunaprevir,[5] danoprevir,[6] paritaprevir,[7] and glecaprevir,[8] with the latter given as a combination with pibrentasvir to treat all forms of Hepatitis C. It is also present in a number of antibacterials,[9] anti-cancer agents,[10,11] and anti-platlet aggregating agents.[12]

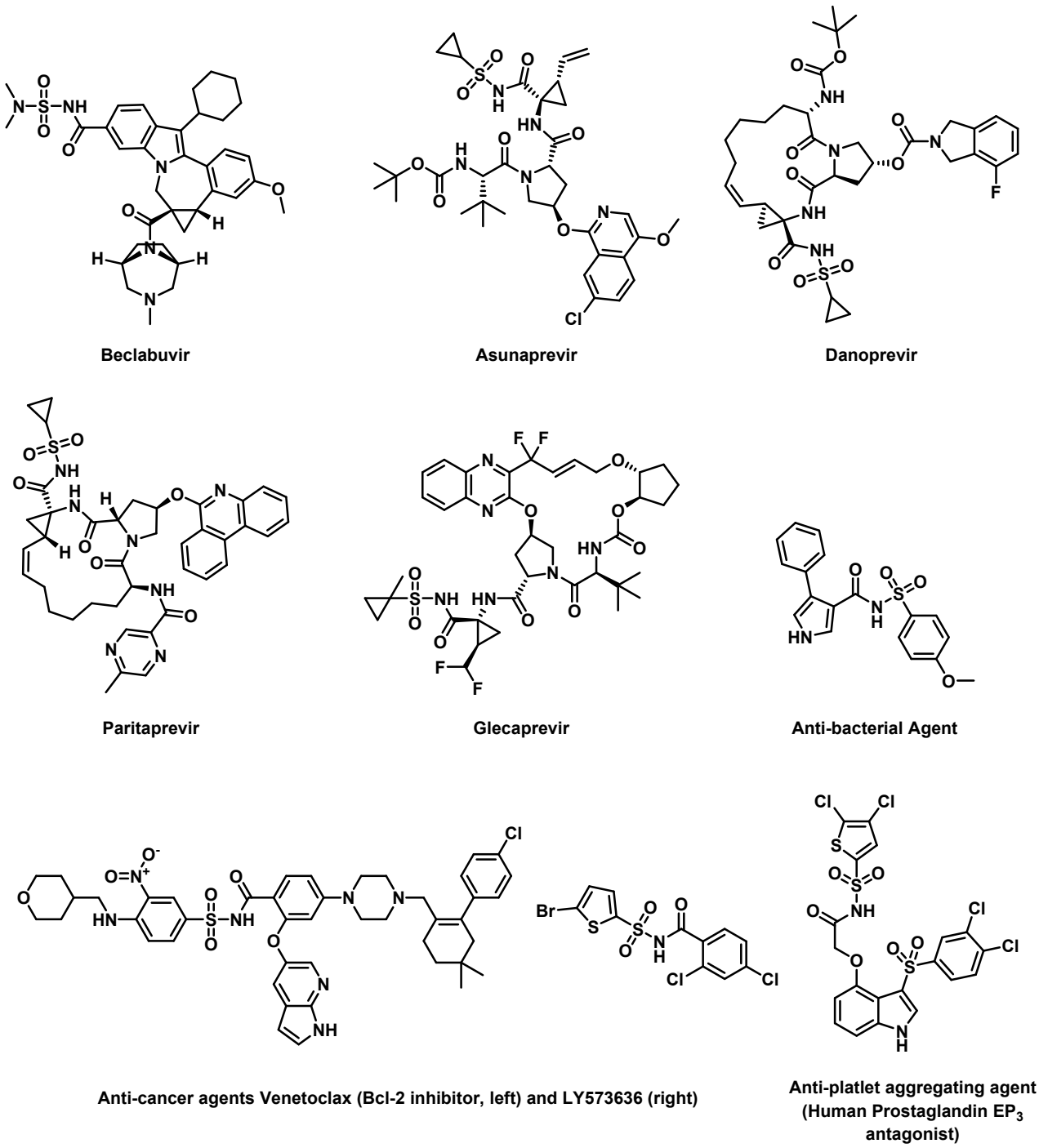


Figure 1. Marketed drugs and pre-clinical compounds containing the acylsulfonamide moiety.

Their prevalence has therefore spurred interest in the discovery of novel and reliable synthetic methods for their preparation. The most commonplace method is coupling acyl chlorides with sulfonamides[13] or carboxylic acids with sulfonamides with the aid of coupling reagents such as EDCI.[14] There has however, been a shift away from these methods as acyl chlorides can be difficult to handle, often requiring strictly anhydrous conditions to avoid hydrolysis. While

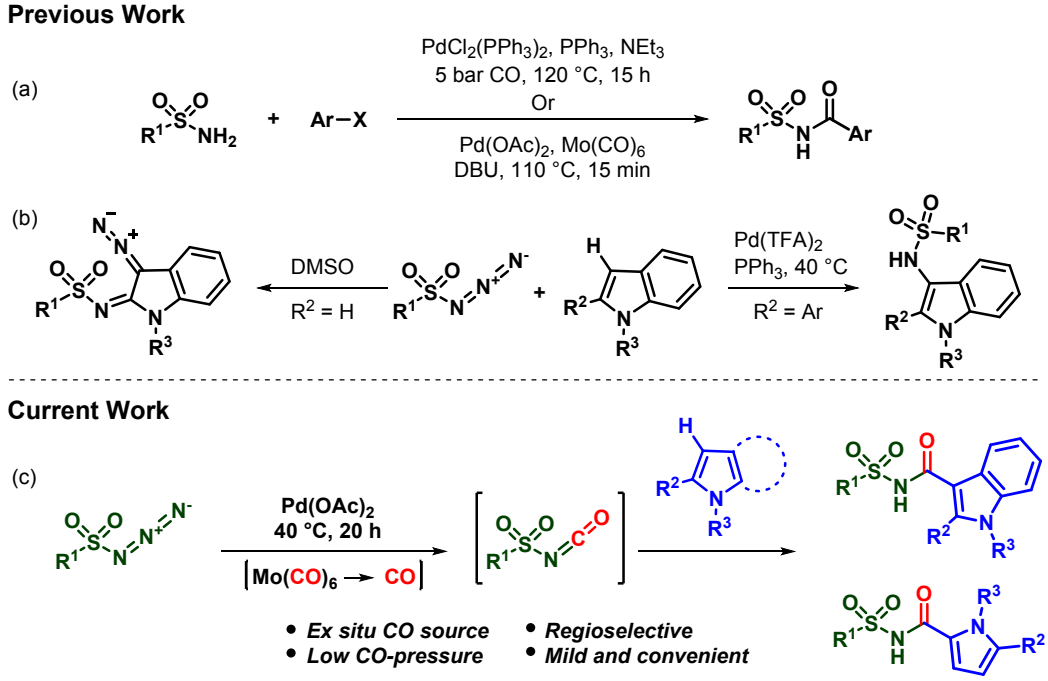
coupling reagents can give satisfactory yields, they can lead to excessive waste and certain by-products such as DCU can be difficult to remove. Reactive sulfonyl isocyanates have also been employed but their hydrolytic instability also lends itself to handling difficulties and consequently, a lack of derivatives that are commercially available.[15]

Recently, sulfonyl azides have been employed instead of sulfonamides, which can be easily synthesized from their corresponding sulfonyl chlorides[16] or amides.[17] This has resulted in the development of new methods including reactions with alkynes[18] and, interestingly, carboxylic acids *via* an *in situ* formed selenocarboxylate.[19] Shangguan and coworkers have also discovered a simple method of reacting thioacids with sulfonyl azides in good yields.[20] More recently, Fang *et al* described a novel method involving the catalytic coupling of carboxylic acids and sulfonyl azides by $Co(CO)_8$ with a rather broad substrate scope but requiring harsher conditions.[21]

Palladium-catalyzed carbonylative syntheses are a convenient means of preparing a range of carbonyl derived functional groups such as carbamates, ureas, amides and imides.[22] This approach is particularly useful for preparing isotopically labelled target molecules by employing isotopically modified carbon monoxide (i.e. labelled with carbon-11, carbon-13 or carbon-14).[23–25] The carbonylative synthesis of acylsulfonamides via the coupling of aryl halides with alkyl and aryl sulfonamides has been previously reported (Scheme 1).[26,27] However these methods employ harsh conditions, lead to the formation of halide salt waste and, in the work of Schnyder *et al*,[27] involve the use of palladium ligands and elevated CO-pressures. Based on previous efforts on the carbonylative coupling of sulfonyl azides,[28–31] we envisioned an efficient route to 3-acyl indole and 2-acyl pyrrole derivatives *via* the *in situ* formation and subsequent capture of a sulfonyl isocyanate intermediate by an electron-rich heterocycle. A literature survey revealed precedent for the direct reaction between sulfonyl azides and indoles through a cycloaddition and subsequent ring-opening cascade[32] or a palladium-catalyzed *N*-

arylation process[33] both of which presented potential synthetic challenges. Herein we describe the development of palladium catalyzed synthesis of acylsulfonamides *via* the carbonylative acylation of indole and pyrrole nucleophiles with sulfonyl azides (Scheme 1). Notably, the reaction allows mild and efficient access to new chemical space, is more environmentally benign compared to previous carbonylation methods relying on the use of aryl halides, is compatible with low CO-pressures and convenient *ex situ* CO-generation and does not require the addition of base or external palladium ligands. To the best of our knowledge, this is also the first example of the carbonylation of an azide substrate with a carbon-based nucleophile.

Scheme 1. Previous and present work on the carbonylative synthesis of *N*-acylsulfonamides and known reactions between indoles and sulfonyl azides.



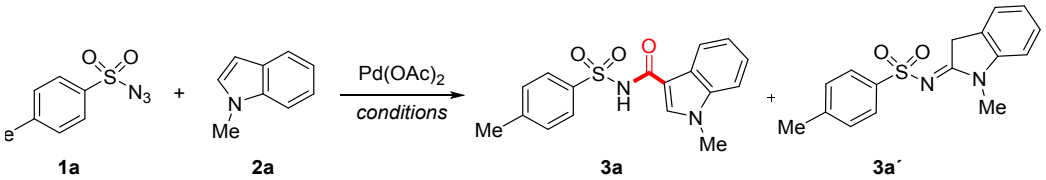
RESULTS AND DISCUSSION

The optimization of reaction conditions (Table 1) began using tosyl azide (**1a**) and 1-methylindole (**2a**) as model substrates with $Pd(OAc)_2$ as the catalyst and MeCN as the

solvent/ligand.[29] The reaction setup followed that of our previous studies: a two-chamber setup was employed consisting of a carbonylation chamber and a CO-generation chamber to produce CO gas *ex situ via* DBU mediated ligand displacement with $Mo(CO)_6$.

Pleasingly, this led to the formation of the desired product in 56% yield (entry 1). During our initial investigations, formation of the competing indolin-2-imine side-product **3a´**[32] was observed (LCMS analysis) even prior to the addition of catalyst. In order to overcome this problem, it was necessary to mix the azide and indole in the final stages of the reaction set-up. This practical adjustment coupled with a modulations of reagent stoichiometry (entries 2 and 3) led to a significant improvement in yield, with the best result obtained using a slight excess of **1a** (85%, entry 2). An increase in CO concentration was trialed with no improvement (entry 4) and a reduction in catalyst loading (entry 5) led to a slight decline in yield. The use of mixed solvent systems for the carbonylation chamber (entries 6 and 7) were also investigated. While the use of MeCN was thought to be required as a ligand for the palladium-catalysed carbonylative coupling process, the complete loss of reactivity when THF was used as a co-solvent was surprising. Accordingly, the use of 1,4-dioxane as a solvent also afforded no product (not shown). Surveying of different temperatures (entries 8 to 10) resulted in a marked decrease in yield to 14% when performed at room temperature and no significant change for an increase in temperature to 65 °C. This did however, afford the option of increasing the reaction temperature during analogue synthesis when employing less-reactive substrates. Finally, the use of anhydrous MeCN (entry 11) in the carbonylation chamber led to the formation of **3a** in an improved in yield of 95%. This is likely due to suppression of the competing hydrolytic degradation of the sulfonyl isocyanate intermediate due to the absence of water.

Table 1. Optimization of reaction conditions[a]



1a **2a** **3a** **3a´**

entry	time (h)	temp (°C)	**1a** equiv	**2a** equiv	solvent	yield (%)[b]
1	20	40	1	1	MeCN	56
2	20	40	1.3	1	MeCN	85
3	20	40	1	1.3	MeCN	75
4[c]	20	40	1.3	1	MeCN	85
5[d]	20	40	1.3	1	MeCN	80
6	20	40	1.3	1	1:9 MeCN:THF	-
7	20	40	1.3	1	1:1 MeCN:THF	-
8	20	65	1.3	1	MeCN	84
9	20	40	1.3	1	MeCN	85
10	20	rt	1.3	1	MeCN	14
11	20	40	1.3	1	Dry MeCN	95

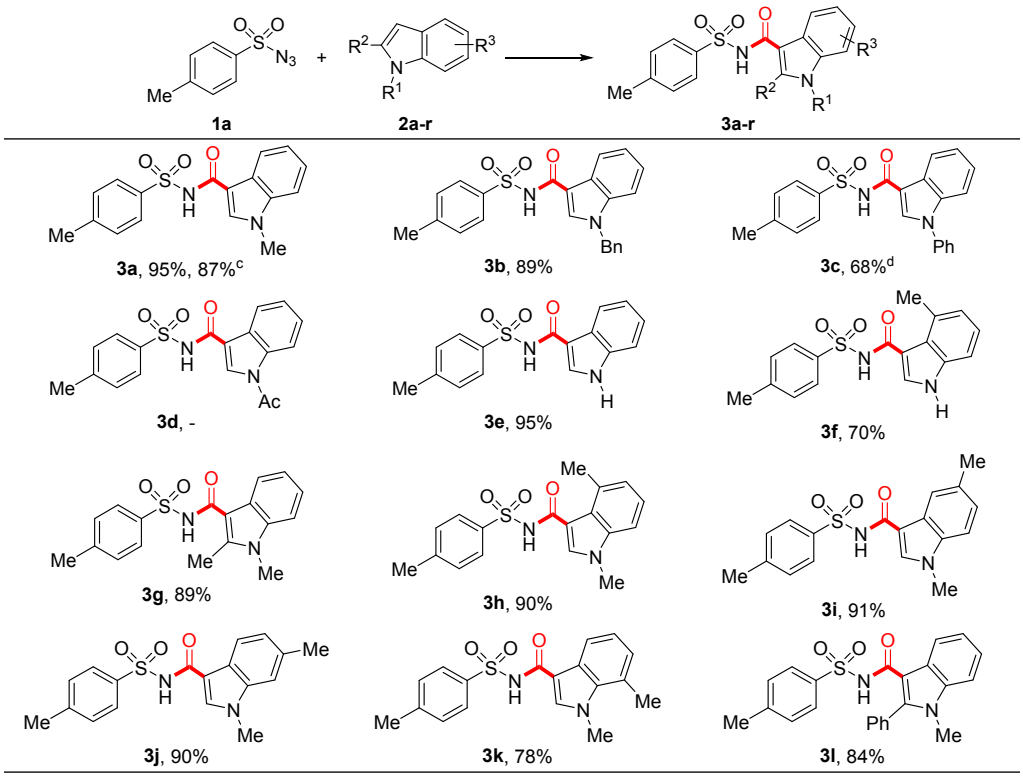
[a] **Reagents and conditions**: (a) Carbonylation chamber 1: *N*-methylindole (0.5 mmol), Tosyl azide (1.3 equiv), 5 mol% $Pd(OAc)_2$, 2 mL solvent; CO-generation chamber: $Mo(CO)_6$ (0.6 equiv), DBU (1.5 equiv), MeCN (2 mL). [b] Isolated yield. [c] 0.8 equiv and 2.4 equiv of $Mo(CO)_6$ and DBU used respectively. [d] 2 mol% $Pd(OAc)_2$.

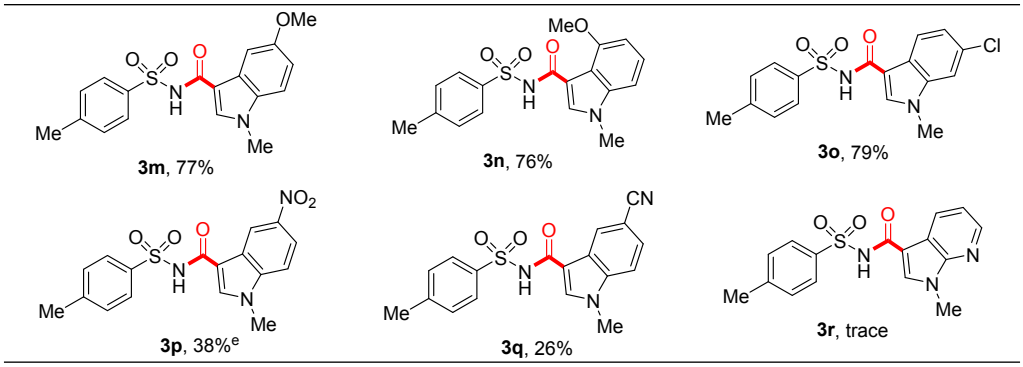
The reaction conditions in entry **11** were employed for the synthesis of a small library of analogues and, in all cases, purification was achieved by column chromatography or recrystallization without the need for a laborious workup. Initially, the scope and limitations of the indole component was examined using a set of substrates with varying electronic and steric properties (Table 2). Substitution on the heterocyclic nitrogen (**3a-3f)** gave yields that correlated well with electronic effects and the more electron-rich analogues **3a** and **3b** gave high yields of 95% and 89%, respectively. The introduction of an electron-withdrawing acyl group completely abolished reactivity (**3d**) as did the presence of a Boc-group (not shown). Substitution with a phenyl group in entry **3c** resulted in an interesting middle ground where, unlike other electron deficient indoles, the reaction proceeded to completion and the desired product was isolated in good yield of 68%. Pleasingly, the presence of a free N-H group was also well-tolerated with indole and 6-methyl indole affording acylsulfonamides **3e** and **3f** in

95% and 70% yields, respectively. This may be due to the absence of a strong base, which could lead to deprotonation of the nitrogen, thereby increasing its nucleophilicity.[34]

Varying the methyl group position resulted in no discernable difference in the reaction outcome (**3g** to **3k**). Notably, the introduction of a bulky 2-phenyl substituent was also well-tolerated and the highly sterically congested **3l** was obtained in 84% yield. Indoles containing electron-donating groups (**3m** and **3n**) performed well as substrates, giving yields of 77% and 76% respectively. A similar yield was also obtained in the presence of a moderately electron-withdrawing chloro group (**3o**, 79%). In accordance with their decreased nucleophilicity, substrates bearing strongly electron-withdrawing nitro- and cyano- groups were found to be less reactive furnishing **3p** and **3q** in moderate yields. Unfortunately, the carbonylative coupling of 7-aza indole (**3r**) did not result in product formation, even under more forcing reaction conditions.

Table 2. Substrate scope for the synthesis of indole analogues[a,b]



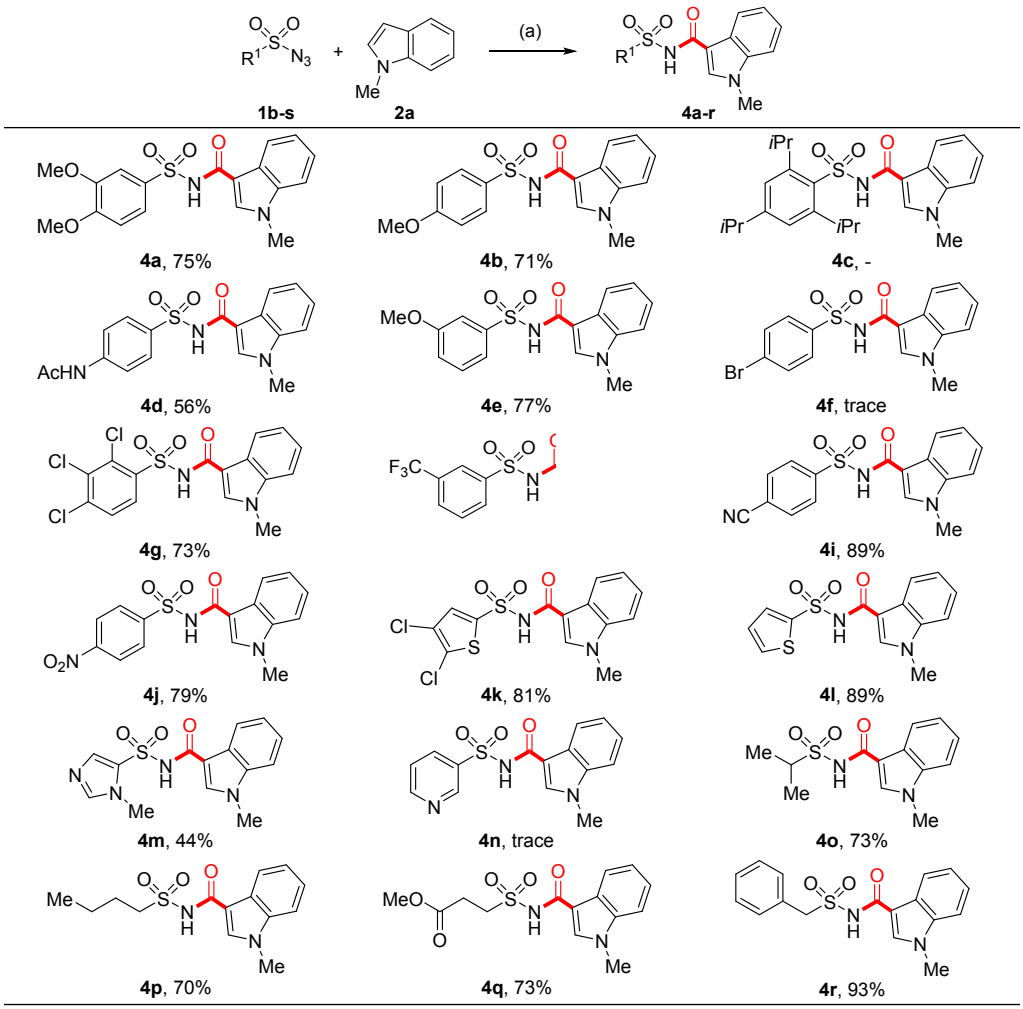


[a] **Reagents and conditions**: (a) Carbonylation chamber: Indole (0.5 mmol), Tosyl azide (1.3 equiv), 5 mol% $Pd(OAc)_2$, Dry MeCN (2 mL); CO-generation chamber: $Mo(CO)_6$ (0.6 equiv), DBU (1.5 equiv), MeCN (2 mL); N_2, 40°C, 20 h. [b] Isolated yields. [c] 1.03 mmol scale [d] 9 days. [e] Nitroindole (3 equiv) and tosyl azide (1 equiv).

Next, we turned our attention to exploring the scope of the reaction with respect to the sulfonyl azide component (Table 3). Importantly, the majority of these analogues could be easily purified from their reaction mixtures by filtration followed by precipitation or recrystallization. With the exception of the bromo analogue **4f**, the reaction was generally compatible with sulfonyl azides containing electron-donating (**4a**, **4b, 4d**) or electron-withdrawing groups (**4e**, **4g**, **4h**, **4i**, **4j**) to give the corresponding acylsulfonamides in good to excellent yields (56% - 92%). The presence of an *ortho*-chloro substituent (**4g**) was also well-tolerated, however the introduction of two *ortho*-isopropyl groups (**4c**) was deleterious for the reaction indicating an upper-limit for acceptance of steric bulk. Pleasingly, heteroaryl azides were also found to be productive substrates affording moderate to good yields of the diheterocyclic derivatives **4k**, **4l** and **4m**. The presence of a basic and potentially coordinating nitrogen (**4m** and **4n**) was detrimental to the reaction and, in the case of **4n**, only trace amounts of the pyridine derivative **4n** were observed (LCMS analysis). Notably, the reaction scope could be extended beyond aryl sulfonyl azides with aliphatic and benzylic sulfonyl azides returning good yields of the corresponding sp^3-carbon linked products (**4o**, **4p**, **4q** and **4r**). Finally, we explored the use of alkyl and aryl azide containing substrates, however no conversion to the desired products was observed under our reaction conditions. This is somewhat surprising given the successful

carbonylative coupling of azide derivatives and may be due to more electron-deficient nature of sulfonyl azides.[35–37]

Table 3. Sulfonyl azide scope for the synthesis of acylsulfonamides[a,b]

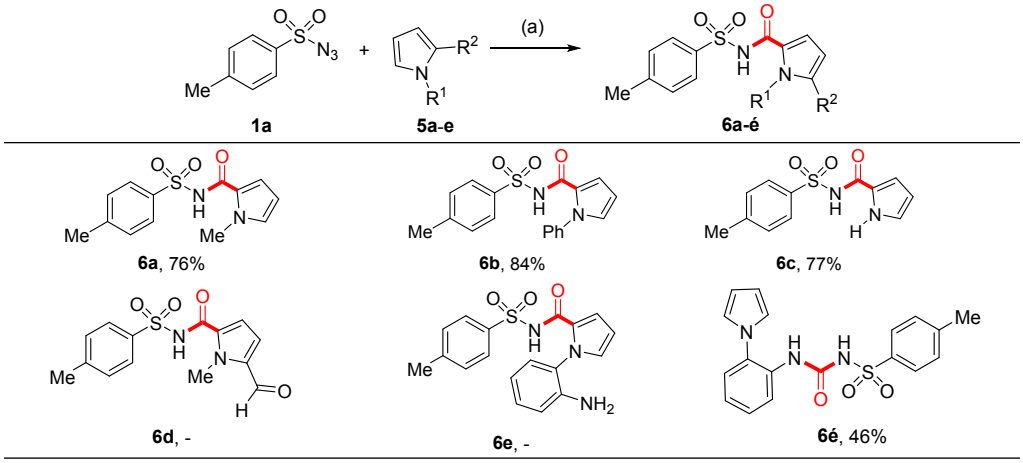


[a] **Reagents and conditions**: (a) Carbonylation chamber: 1-methylindole (0.5 mmol), sulfonyl azide (1.3 equiv), 5 mol% $Pd(OAc)_2$, Dry MeCN (2 mL); CO-generation chamber: $Mo(CO)_6$ (0.6 equiv), DBU (1.5 equiv), MeCN (2 mL); N_2, 40°C, 20 h. [b] Isolated yields.

To further extend the scope of the developed method, the use of pyrrole nucleophiles was investigated (Table 4). Pyrroles bearing *N*-methyl and *N*-phenyl groups were efficiently coupled with tosyl azide and the target compounds **6a** and **6b** were obtained in good yields. Similarly, a free N-H group was also well tolerated (**6c**), however the introduction of an electron-withdrawing formyl group (**6d**) completely abolished reactivity. Finally, the ambident nucleophile **6e** was used to explore chemoselectively and resulted in almost exclusive formation

of sulfonyl urea derivative **6é**, indicating a significant preference for aminocarbonylation[30] over pyrrole acylation under these conditions.

Table 4. Exploring pyrrole derived nucleophiles[a,b]



[a] **Reagents and conditions**: (a) Carbonylation chamber: 1-methylindole (0.5 mmol), sulfonyl azide (1.3 equiv), 5 mol% $Pd(OAc)_2$, Dry MeCN (2 mL); CO-generation chamber: $Mo(CO)_6$ (0.6 equiv), DBU (1.5 equiv), MeCN (2 mL); N_2, 40°C, 20 h. [b] Isolated yields.

Based on our previous studies[29,30,38] and the work of others,[35–37] a plausible reaction mechanism is depicted in Figure 2. Firstly, the Pd(II) pre-catalyst is reduced to the active Pd(0) species, presumably under the action of CO.[39] This is supported by control reactions conducted in the absence of or with sub-stoichiometric amounts of CO, which led to no product formation or incomplete conversion to the acyl sulfonamide product and direct *N*-heteroarylation, respectively. Oxidative addition of the palladium center to the sulfonyl azide substrate generates the nitrene intermediate (A in Figure **2**) and carbon monoxide coordination followed by migratory insertion leads to the key sulfonyl isocyanate intermediate (B in Figure **2**). Finally, nucleophilic attack by an indole or pyrrole derivative generates the final acyl sulfonamide products. Control experiments support the intermediacy of a sulfonyl isocyante as the reaction of tosyl amide with *N*-methylindole led to no product formation while the direct reaction of tosyl isocyanate with 1-methylindole gave acyl sulfonamide **3a** in 68% yield.

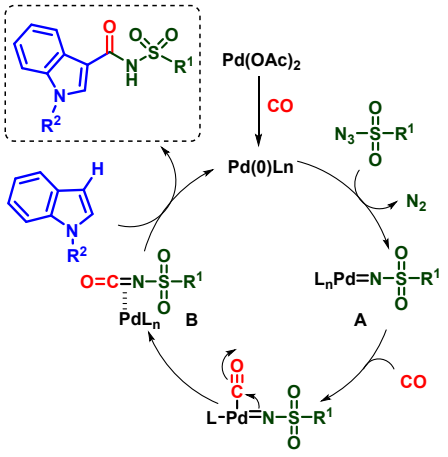


Figure 2. Plausible mechanism for the synthesis of *N*-acylsulfonamides. L = MeCN or CO

A brief investigation into the utility of the method for isotopic labelling was performed by employing [^{11}C]CO to synthesize the acyl sulfonamide **[^{11}C]3a** (Figure **3**). Compounds labelled with carbon-11, a positron emitting radionuclide with a half-life of 20.4 min, could be used as radiotracers in biomedical research and clinical routine with positron emission tomography (PET). Carbonylation with [^{11}C]CO differs from the standard transition-metal-catalyzed carbonylation as the rapid physical decay of the radionuclide necessitate very short reaction times, typically less than 10 min, so as to not compromise radiochemical yields. This prerequisite is helped by the minute quantities of [^{11}C]CO employed in labelling reactions, typically in the range of 10-50 nmol. The high molar activity (GBq/µmol) of cyclotron produced carbon-11 and the high sensitivity of PET scanners, enables administration of labelled compounds at trace quantities (a few nanomoles), for most compounds well below the pharmacologically active dose. The labelling reactions are optimized with regards to [^{11}C]CO, and all other reagents, including the catalyst, are employed in large excess de facto, ruling out a propagating catalytic cycle.

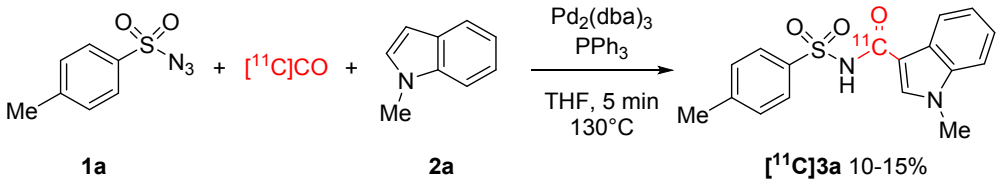


Figure 3. Synthesis of **[^{11}C]3a** by palladium mediated (0.67 equiv $Pd_2(dba)_3$ relative to **1a**) carbonylation with [^{11}C]CO.

The optimized reaction conditions for **3a** were used as the starting point and [^{11}C]CO was transferred to the reaction vial in a stream of xenon. The remarkable solubility of the transfer gas in the reaction solvent facilitated high recovery of [^{11}C]CO at ambient pressure conditions while using a non-vented vial.[28,40–43] Initially, the desired product **[^{11}C]3a** was not observed but when increasing the temperature to 90°C or 120°C the product was detectable by radio-HPLC analysis. However, at these elevated temperatures the reaction mixture was heterogeneous and accurate quantification was not possible due to low recovery of radioactive material from the HPLC column. It was also suspected that due to the minute amounts of [^{11}C]CO used, it could be partially consumed in a process where Pd(II) was reduced to Pd(0)-species via the water-gas-shift-reaction.[44,45] This result was in agreement with control reactions conducted with sub-stoichiometric amounts of isotopically unmodified CO and further studies with Pd(II) pre-catalysts was therefore abandoned.

Instead, the reaction was carried out using a Pd(0) source ($Pd_2(dba)_3$) and PPh_3 as a ligand at 120°C for 5 min. Gratifyingly, compound **[^{11}C]3a** was obtained in 2.4% radiochemical yield and when the temperature was increased to 140°C, the yield was slightly improved (5.2%), however this was accompanied by palladium black precipitation. At 130°C the product was obtained in 10% and 15% radiochemical yield (n=2) with good product selectivity (57% and 73%) and moderate conversion of [^{11}C]CO (18% and 21%). The compound was identified by

analytical radio-UV-HPLC and co-elution of **[^{11}C]3a** (radio trace) with the reference compound **3a** (UV-trace). In comparison with the method optimized for CO, the substochiometric amounts of [^{11}C]CO required the Pd(II)-precatalyst to be exchanged for a catalytically active Pd(0)-complex and the reaction temperature significantly increased for the reaction kinetics to match the short timeframe given by the half-life of carbon-11. Importantly, the identified labelling conditions provide sufficient quantities of **[^{11}C]3a** to enable pre-clinical PET evaluation and are excellent starting point for further investigations into the synthesis of ^{11}C-labelled *N*-acylsulfonamides.[46] Moreover, this is to the best of our knowledge, the first reported example of a C-H bond acylation reaction using [^{11}C]CO.

CONCLUSION

In summary, a mild and convenient method for the carbonylative synthesis of valuable acyl sulfonamide products has been developed. The combination of *in situ* isocyanate generation from a convenient solid CO-source, ligand-free catalyst system and regioselective acylation make this an attractive synthetic strategy. Moreover, its efficiency has been demonstrated through the synthesis of 34 analogues in yields of up to 95% using a diverse array of indoles, pyrroles and sulfonyl azides. The methodology was also successfully modified for carbon-11 labelling, exemplified by **[^{11}C]3a** which was obtained in 10-15% radiochemical yield. This work further highlights the utility of sulfonyl azides in carbonylative syntheses and provides a valuable tool for the synthesis of this important and pharmaceutically relevant class of compounds.

EXPERIMENTAL

General information. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F-254 plates and visualized with UV light. Flash column chromatography was performed on silica gel 60 (40-63 μm). ^{1}H and $^{13}C\{1H\}$ spectra were recorded at 400 and 100 MHz, respectively. The chemical shifts for ^{1}H NMR and $^{13}C\{1H\}$ NMR are referenced to TMS *via* residual solvent signals (^{1}H: CD_3OD at 3.31 ppm, $CDCl_3$ at 7.26 ppm and DMSO-d_6 at 2.50 ppm; $^{13}C\{1H\}$: CD_3OD at 49.0 ppm, $CDCl_3$ at 77.16 ppm and DMSO-d_6 at 39.52 ppm). Analytical HPLC/ESI-MS was performed using electrospray ionization (ESI) and a C18 column (50×3.0 mm, 2.6 μm particle size, 100 Å pore size) with CH_3CN/H_2O in 0.05% aqueous HCOOH as mobile phase at a flow rate of 1.5 ml/min. LC purity analyses were run using a gradient of 5-100% CH_3CN/H_2O in 0.05% aqueous HCOOH as mobile phase at a flow rate of 1.5 ml/min for 5 mins unless otherwise stated on a C18 column. High resolution molecular masses (HRMS) were determined on a mass spectrometer equipped with an ESI source and time-of-flight (TOF) or Fourier transform-ion cyclotron resonance mass analyzer as indicated.

General Procedure for the Synthesis of sulfonyl azides as exemplified by the synthesis of methyl 3-(azidosulfonyl)propanoate (1r): A solution of methyl 3-(chlorosulfonyl)propanoate (312 mg, 1.67 mmol) in acetone (10 mL) was added dropwise to a solution of sodium azide (173 mg, 2.66 mmol) in water (3 mL) in a round-bottom flask. After 20 h, the solution was added to water (30 mL) and extracted with EtOAc (3 × 25 mL). The combined organic layers were washed with water (25 mL) followed by saturated $NaHCO_3$ solution (25 mL), dried with brine and $MgSO_4$, filtered and the resulting solution evaporated in vacuo to give methyl 3-(azidosulfonyl)propanoate as a clear oil (259 mg, 80%). ^{1}H NMR ($CDCl_3$) δ 3.75 (s, 3H), 3.66 (t, J = 7.3 Hz, 2H), 2.91 (t, J = 7.3 Hz, 2H); $^{13}C\{1H\}$ NMR ($CDCl_3$) δ 170.0 (C), 52.8 (CH_2), 51.1 (CH_2), 28.4 (CH_3)**;** HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_4H_7N_3O_4SNa$ 216.0050: Found 216.0049.

2,3,4-trichlorobenzenesulfonyl azide (1h): Yellow liquid (274 mg, 66%). ^{1}H NMR ($CDCl_3$) δ 7.99 (d, J = 8.7 Hz, 2H), 7.61 (d, J = 8.7 Hz, 2H); ^{13}C{1H} NMR ($CDCl_3$) δ 141.2 (C), 136.9 (C), 135.46 (C), 133.2 (C), 129.4 (CH), 128.7 (CH)**.**

1-Methyl-1*H*-imidazole-4-sulfonyl azide (1n): Clear crystals (435 mg, 82%). ^{1}H NMR ($CDCl_3$) δ 7.62 (d, J = 1.3 Hz, 1H), 7.57 (d, J = 1.0 Hz, 1H), 3.80 (s, 3H); ^{13}C{1H} NMR ($CDCl_3$) δ 140.0 (CH), 139.0 (C), 125.7 (CH), 34.4 (CH_3); M.P: 60 – 62 °C; HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_4H_5N_5O_2SNa$ 210.0056: Found 210.0057.

General Procedure for the Synthesis of *N*-Acylsulfonamides as exemplified by the synthesis of 1-methyl-*N*-tosyl-1*H*-indole-3-carboxamide (3a): *N*-Methylindole (53.4 mg, 0.407 mmol) and tosyl azide (104 mg, 0.529 mmol) were weighed in separate vials. Palladium (II) acetate (4.5 mg, 0.02 mmol) was added to the reaction chamber of an oven-dried H-tube (carbonylation chamber) and $Mo(CO)_6$ (65.6 mg, 0.248 mmol) to the CO generating chamber (CO-generation chamber). The azide and indole were then added to carbonylation as a solution in dry acetonitrile (2 mL), both chambers were then capped and the entire system purged twice with N_2 gas. 1,8-Diazabicyclo(5.4.0)undec-7-ene (93 µL, 0.622 mmol) was finally added as an MeCN solution (2 mL) *via* syringe to commence CO generation. The reaction was then stirred vigorously at 40^{o}C for 20 h. The contents of the carbonylation chamber were then purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as light-orange crystals (127 mg, 95%. 1.03 mmol scale 295 mg, 87%). ^{1}H NMR (DMSO-d_6) δ 11.85 (br s, 1H), 8.35 (s, 1H), 7.94 – 7.83 (m, 1H), 7.94 – 7.83 (m, 2H), 7.55 – 7.48 (m, 1H), 7.46 – 7.38 (m, 2H), 7.25 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.17 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 3.84 (s, 3H), 2.38 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 143.7 (C), 137.5 (C), 136.9 (C), 135.4 (CH), 129.4 (2×CH), 127.6 (2×CH), 126.5 (C), 122.8 (CH), 121.8 (CH), 120.8 (CH), 110.8 (CH), 106.5 (C), 33.4 (CH_3), 21.1 (CH_3); mp: 195 – 197 °C; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{17}H_{15}N_2O_3S$ 327.0803: Found 327.0802; LC purity (254 nm) = >99%.

1-Benzyl-N-tosyl-1H-indole-3-carboxamide **(3b)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) and recrystalisation from hot minimal MeCN to give the product as pale yellow crystals (140 mg, 89%). ^{1}H NMR (DMSO-d_6) δ 11.94 (s, 1H), 8.49 (s, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.3 Hz, 2H), 7.38 – 7.27 (m, 5H), 7.24 – 7.12 (m, 2H), 5.48 (s, 2H), 2.38 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 143.8 (C), 137.4 (C), 136.8 (C), 136.2 (C), 134.9 (CH), 129.4 (2×CH), 128.7 (2×CH), 127.8 (CH), 127.6 (2×CH), 127.5 (2×CH), 126.6 (C), 122.9 (CH), 121.9 (CH), 120.9 (CH), 111.1 (CH), 107.1 (C), 49.8 (CH_2), 21.1 (CH_3); mp: 233 – 234 °C; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{19}N_2O_3S$ 403.1116: Found 403.1121; LC purity (254 nm) = >99%.

1-Phenyl-N-tosyl-1H-indole-3-carboxamide **(3c)**: Was stirred at 40 ˚C for 9 days instead of 20 h. Purified by column chromatography (20:80:0.1 to 50:50:0.1 Pentane:EtOAc:HCOOH) followed by recrystalisation in hot MeCN to give the product as white crystals (116 mg, 68%). ^{1}H NMR (DMSO-d_6) δ 12.00 (br s, 1H), 8.71 (s, 1H), 8.14 – 8.06 (m, 1H), 7.93 (d, J = 8.3 Hz, 2H), 7.69 – 7.61 (m, 4H), 7.56 – 7.49 (m, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.31 – 7.23 (m, 2H), 2.39 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 143.9 (C), 137.8 (C), 137.2 (C), 135.7 (C), 134.3 (CH), 130.1 (2×CH), 129.5 (2×CH), 127.9 (CH), 127.7 (2×CH), 127.0 (C), 124.3 (2×CH), 123.9 (CH), 122.7 (CH), 121.3 (CH), 111.2 (CH), 108.9 (C), 21.1 (CH_3); M.P: 206 – 208 °C; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{22}H_{17}N_2O_3S$ 389.0960: Found 389.0972; LC purity (254 nm) = 98%.

N-Tosyl-1H-indole-3-carboxamide **(3e)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as a dark brown solid (120 mg, 95%). ^{1}H NMR (DMSO-d_6) δ 11.94 (s, 1H), 11.84 (s, 1H), 8.38 (d, J = 3.2 Hz, 1H), 7.98 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.48 – 7.39 (m, 3H), 7.18 (ddd, J = 8.2, 7.2, 1.3 Hz, 1H),

7.12 (ddd, J = 8.0, 7.1, 1.1 Hz, 1H), 2.38 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.9, 143.7, 137.5, 136.2, 131.7 (CH), 129.4 (2×CH), 127.6 (2×CH), 126.1 (C), 122.8 (CH), 121.5 (CH), 120.7 (CH), 112.2 (CH), 107.6 (C), 21.1 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{16}H_{13}N_2O_3S$ 313.0647: Found 313.0643; LC purity (254 nm) = >99%

4-Methyl-N-tosyl-1H-indole-3-carboxamide **(3f)**: Purified by column chromatography (65:30:5:0.1 Pentane:EtOAc:Toluene:HCOOH) to give the product as a purple oil (100 mg, 70%). ^1H NMR (DMSO-d_6) δ 11.87 (s, 2H), 8.08 (d, J = 3.1 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.1 Hz, 1H), 7.11 – 7.02 (m, 1H), 6.85 (d, J = 7.2 Hz, 1H), 2.43 (s, 3H), 2.39 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 162.4 (C), 143.6 (C), 137. (2×C), 136.9 (C), 132.2 (CH), 130.6 (C), 129.4 (2×CH), 127.5 (2×CH), 124.2 (C), 123.0 (CH), 122.8 (CH), 109.9 (CH), 109.6 (C), 21.7 (CH_3), 21.1 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{17}H_{15}N_2O_3$ 327.0803: Found 327.0792; LC purity (254 nm) = >99%.

1,2-Dimethyl-N-tosyl-1H-indole-3-carboxamide **(3g)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as a beige solid (126 mg, 89%). ^1H NMR (DMSO-d_6) δ 11.64 (br s, 1H), 7.95 (d, J = 8.3 Hz, 2H), 7.80 – 7.74 (m, 1H), 7.52 – 7.46 (m, 1H), 7.43 (d, J = 8.3 Hz, 2H), 7.23 – 7.16 (m, 2H), 3.67 (s, 3H), 2.56 (s, 3H), 2.39 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 163.2 (C), 144.1 (C), 143.6 (C), 137.7 (C), 136.1 (C), 129.4 (2×CH), 127.7 (2×CH), 125.3 (C), 121.9 (CH), 121.1 (CH), 119.7 (CH), 110.1 (CH), 105.7 (C), 29.6 (CH_3), 21.1 (CH_3), 11.8 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{17}N_2O_3S$ 341.0960: Found 341.0963; LC purity (254 nm) = >99%.

1,4-Dimethyl-N-tosyl-1H-indole-3-carboxamide **(3h)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) and recrystalisation from minimal MeCN to give the product as colorless crystals (144 mg, 87%). ^1H NMR (DMSO-d_6) δ 11.89 (s, 1H), 8.10 (s, 1H), 7.92 – 7.86 (m, 2H), 7.46 – 7.40 (m, 2H), 7.32 (dt, J = 8.3, 0.9 Hz, 1H), 7.14 (dd, J = 8.3,

7.2 Hz, 1H), 6.91 (dt, *J* = 7.2, 1.0 Hz, 1H), 3.81 (s, 3H), 2.43 (s, 3H), 2.39 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 162.1 (C), 143.6 (C), 137.4 (C), 137.4 (C), 136.0 (CH), 130.8 (C), 129.4 (2×CH), 127.5 (2×CH), 124.6 (C), 123.3 (CH), 122.8 (CH), 108.5 (C), 108.2 (CH), 33.2 (CH_3), 21.5 (CH_3), 21.1 (CH_3); mp: 117 – 119 °C; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{17}N_2O_3S$ 341.0960: Found 341.0968; LC purity (254 nm) = >99%.

1,5-Dimethyl-N-tosyl-1H-indole-3-carboxamide **(3i)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) and recrystalisation from minimal hot MeCN to give the product as a light-orange solid (150 mg, 91%). ^{1}H NMR (DMSO-d_6) δ 11.80 (br s, 1H), 8.28 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 2H), 7.78 (s, 1H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.7 Hz, 1H), 7.07 (d, *J* = 7.9 Hz, 1H), 3.80 (s, 3H), 2.38 (s, 3H), 2.36 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 143.7 (C), 137.5 (C), 135.3 (CH), 135.3 (C), 130.8 (C), 129.4 (2×CH), 127.6 (2×CH), 126.8 (C), 124.2 (CH), 120.5 (CH), 110.4 (CH), 106.0 (C), 33.4 (CH_3), 21.1 (CH_3), 21.0 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{17}N_2O_3S$ 341.0960: Found 341.0956; LC purity (254 nm) = >99%.

1,6-Dimethyl-N-tosyl-1H-indole-3-carboxamide **(3j)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give a light-brown solid (149 mg, 90%). ^{1}H NMR (DMSO-d_6) δ 11.82 (br s, 1H), 8.27 (s, 1H), 7.89 (d, *J* = 8.3 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 2H), 7.30 (s, 1H), 7.00 (d, *J* = 8.2 Hz, 1H), 3.79 (s, 3H), 2.40 (s, 3H), 2.37 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 143.7 (C), 137.5 (C), 137.3 (C), 134.9 (CH), 132.2 (C), 129.4 (2×CH), 127.6 (2×CH), 124.3 (C), 123.5 (CH), 120.5 (CH), 110.5 (CH), 106.4 (C), 33.3 (CH_3), 21.3 (CH_3), 21.0 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{17}N_2O_3S$ 341.0960: Found 341.0957; LC purity (254 nm) = >99%.

1,7-Dimethyl-N-tosyl-1H-indole-3-carboxamide **(3k)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give a light-brown solid (129 mg, 78%). ^{1}H

NMR (DMSO-d_6) δ 11.78 (s, 1H), 8.23 (s, 1H), 7.89 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 7.8 Hz, 1H), 7.41 (d, J = 8.3 Hz, 2H), 7.00 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 7.1 Hz, 1H), 4.06 (s, 3H), 2.69 (s, 3H), 2.37 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.5 (C), 143.7 (C), 137.5 (C), 136.9 (CH), 135.5 (C), 129.4 (2×CH), 127.6 (C), 127.6 (2×CH), 125.3 (CH), 122.3 (C), 121.9 (CH), 118.9 (CH), 105.9 (C), 37.4 (CH_3), 21.0 (CH_3), 18.9 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{17}N_2O_3S$ 341.0960: Found 341.0966; LC purity (254 nm) = >99%.

1-Methyl-2-phenyl-N-tosyl-1H-indole-3-carboxamide **(3l)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) and recrystalisation from minimal MeCN to give the product as pale yellow crystals (167 mg, 84%). ^{1}H NMR (DMSO-d_6) δ 11.02 (s, 1H), 7.82 – 7.72 (m, 3H), 7.59 (d, J = 8.1 Hz, 1H), 7.56 – 7.47 (m, 3H), 7.45 – 7.35 (m, 4H), 7.31 (ddd, J = 8.3, 7.0, 1.3 Hz, 1H), 7.25 (ddd, J = 8.2, 7.1, 1.1 Hz, 1H), 3.59 (s, 3H), 2.41 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 162.5 (C), 144.0 (C), 143.8 (C), 137.1 (C), 136.5 (C), 130.7 (2×CH), 129.5 (C), 129.3 (3×CH), 128.3 (2×CH), 127.6 (2×CH), 125.5 (C), 122.8 (CH), 121.6 (CH), 120.0 (CH), 110.9 (CH), 107.2 (C), 31.0 (CH_3), 21.1 (CH_3); mp: 181 – 183 °C; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{23}H_{19}N_2O_3S$ 403.1116: Found 403.1106; LC purity (254 nm) = >99%.

5-Methoxy-1-methyl-N-tosyl-1H-indole-3-carboxamide **(3m)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as dark brown solid (112 mg, 80%). ^{1}H NMR (DMSO-d_6) δ 11.84 (br s, 1H), 8.32 (s, 1H), 7.92 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 2.5 Hz, 1H), 7.46 – 7.34 (m, 3H), 6.87 (dd, J = 8.9, 2.5 Hz, 1H), 3.79 (s, 3H), 3.74 (s, 3H), 2.35 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.7 (C), 155.5 (C), 143.7 (C), 137.6 (C), 135.5 (CH), 131.9 (C), 129.5 (2×CH), 127.6 (2×CH), 127.4 (C), 112.9 (CH), 111.6 (CH), 106.1 (C), 102.3 (CH), 55.3 (CH_3), 33.5 (CH_3), 21.0 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{17}N_2O_4S$ 357.0909: Found 357.0920; LC purity (254 nm) = >99%.

4-Methoxy-1-methyl-N-tosyl-1H-indole-3-carboxamide **(3n)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as dark brown crystals (114 mg, 77%). ^{1}H NMR (DMSO-d_6) δ 11.83 (br s, 1H), 8.05 (s, 1H), 7.92 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.3 Hz, 2H), 7.32 – 7.17 (m, 2H), 6.90 (d, J = 7.5 Hz, 1H), 4.08 (s, 3H), 3.79 (s, 3H), 2.39 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 160.1 (C), 150.9 (C), 144.2 (C), 139.0 (C), 137.6 (CH), 136.5 (C), 129.5 (2×CH), 127.7 (2×CH), 123.8 (CH), 112.8 (C), 107.5 (C), 105.4 (CH), 103.4 (CH), 56.3 (CH_3), 33.4 (CH_3), 21.1 (CH_3); mp: 208 – 210 °C; HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{18}H_{17}N_2O_4S$ 357.0909: Found 357.0923; LC purity (254 nm) = >99%.

6-Chloro-1-methyl-N-tosyl-1H-indole-3-carboxamide **(3o)**: Purified by column chromatography (20 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as a brown solid (150 mg, 79%). ^{1}H NMR (DMSO-d_6) δ 11.96 (br s, 1H), 8.36 (s, 1H), 7.95 (d, J = 8.5 Hz, 1H), 7.89 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 1.8 Hz, 1H), 7.42 (d, J = 8.1 Hz, 2H), 7.18 (dd, J = 8.5, 1.9 Hz, 1H), 3.83 (s, 3H), 2.37 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.4 (C), 143.8 (C), 137.4 (C), 137.3 (C), 136.3 (CH), 129.4 (2×CH), 127.6 (C and 2×CH as per HMBC), 125.2 (C), 122.1 (2 CH as per HSQC), 110.9 (CH), 106.8 (C), 33.5 (CH_3), 21.1 (CH_3); HRMS (ESI-TOF) m/z: [M - H]$^-$ Calcd for $C_{17}H_{14}ClN_2O_3S$ 361.0414: Found 361.0405; LC purity (254 nm) = >99%.

1-Methyl-5-nitro-N-tosyl-1H-indole-3-carboxamide **(3p)**: 3 Equiv of indole used instead of 1:1.3 indole:azide.. Purified by column chromatography (50 to 100% EtOAc in pentane and 0.1% HCOOH) and recrystalisation from minimal MeCN to give the product as green crystals (58 mg, 38%). ^{1}H NMR (DMSO-d_6) δ 12.18 (s, 1H), 8.82 (d, J = 1.7 Hz, 1H), 8.55 (s, 1H), 8.19 – 8.04 (m, 1H), 7.91 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 9.1 Hz, 1H), 7.44 (d, J = 8.1 Hz, 2H), 3.92

(s, 3H), 2.39 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.1 (C), 144.0 (C), 142.6 (C), 139.8 (C), 138.8 (CH), 137.0 (C), 129.5 (2×CH), 127.7 (2×CH), 125.8 (C), 118.0 (CH), 117.2 (CH), 111.8 (CH), 108.4 (C), 33.9 (CH_3), 21.1 (CH_3); mp: 238 – 239 °C; HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{17}H_{14}N_3O_5S$ 372.0654: Found 372.0644; LC purity (254 nm) = 98%.

5-Cyano-1-methyl-N-tosyl-1H-indole-3-carboxamide **(3q)**: Purified by column chromatography (25 to 100% EtOAc in pentane and 0.1% HCOOH) to give the product as a beige solid (46 mg, 26%). ^1H NMR (DMSO-d_6) δ 12.10 (br, s, 1H), 8.50 (s, 1H), 8.33 (dd, J = 1.5, 0.5 Hz, 1H), 7.89 (d, J = 8.3 Hz, 2H), 7.77 – 7.72 (m, 1H), 7.63 (dd, J = 8.6, 1.6 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 3.89 (s, 3H), 2.39 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.3 (C), 143.9 (C), 138.6 (C), 137.7 (CH), 137.2 (C), 129.5 (2×CH), 127.6 (2×CH), 126.1 (C), 125.8 (CH), 125.6 (CH), 119.8 (C), 112.5 (CH), 107.3 (C), 104.1 (C), 33.7 (CH_3), 21.1 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{18}H_{14}N_3O_3S$ 352.0756: Found 352.0750; LC purity (254 nm) = >99%.

N-((3,4-Dimethoxyphenyl)sulfonyl)-1-methyl-1H-indole-3-carboxamide **(4a)**: Purified by column chromatography (50 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as maroon crystals (154 mg, 75%). ^1H NMR (DMSO-d_6) δ 11.75 (s, 1H), 8.33 (s, 1H), 8.03 – 7.96 (m, 1H), 7.62 (dd, J = 8.5, 2.2 Hz, 1H), 7.52 (d, J = 8.2 Hz, 1H), 7.49 (d, J = 2.2 Hz, 1H), 7.25 (ddd, J = 8.3, 7.2, 1.3 Hz, 1H), 7.21 – 7.14 (m, 2H), 3.84 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.6 (C), 152.6 (C), 148.2 (C), 136.9 (C), 135.4 (CH), 131.8 (C), 126.5 (C), 122.8 (CH), 121.8 (CH), 121.7 (CH), 120.8 (CH), 111.1 (CH), 110.8 (CH), 110.2 (CH), 106.6 (C), 55.9 (CH_3), 55.8 (CH_3), 33.4 (CH_3); mp: 172 – 174 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}N_2O_5S$ 375.1015: Found 375.1022; LC purity (254 nm) = 98%.

N-((4-Methoxyphenyl)sulfonyl)-1-methyl-1H-indole-3-carboxamide **(4b)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as brown-green crystals (124 mg, 71%). ^{1}H NMR (DMSO-d_6) δ 11.78 (s, 1H), 8.34 (s, 1H), 7.99 (d, J = 7.9 Hz, 1H), 7.98 – 7.90 (m, 2H), 7.51 (d, J = 8.2 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.22 – 7.09 (m, 3H), 3.83 (s, 6H); ^{13}C{1H} NMR (DMSO-d_6) δ 162.8 (C), 161.6 (C), 136.9 (C), 135.4 (CH), 131.8 (C), 129.9 (2×CH), 126.5 (C), 122.8 (CH), 121.8 (CH), 120.8 (CH), 114.1 (2×CH), 110.7 (CH), 106.5 (C), 55.7 (CH_3), 33.4 (CH_3); mp: 177 – 179 °C; HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{17}H_{17}N_2O_4S$ 345.0909: Found 345.0919; LC purity (254 nm) = 99%.

N-((4-Acetamidophenyl)sulfonyl)-1-methyl-1H-indole-3-carboxamide **(4d)**: Purified by dissolving the material in minimal DMF, filtering any black solid (Pd black), and precipitating and washing with MeCN to give the product as a grey solid (104 mg, 56%). ^{1}H NMR (DMSO-d_6) δ 11.82 (br s, 1H), 10.35 (s, 1H), 8.33 (s, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.93 (d, J = 8.7 Hz, 2H), 7.78 (d, J = 8.7 Hz, 2H), 7.51 (d, J = 8.1 Hz, 1H), 7.24 (t, J = 7.6 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 3.83 (s, 3H), 2.08 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 169.0 (C), 161.7 (C), 143.4 (C), 136.9 (C), 135.4 (CH), 133.9 (C), 128.8 (2×CH), 126.5 (C), 122.7 (CH), 121.8 (CH), 120.8 (CH), 118.3 (2×CH), 110.7 (CH), 106.7 (C), 33.3 (CH_3), 24.1 (CH_3); HRMS (ESI-TOF) m/z: [M + H]$^+$ Calcd for $C_{18}H_{18}N_3O_4S$ 372.1018: Found 372.1003; LC purity (254 nm) = >99%.

N-((3-Methoxyphenyl)sulfonyl)-1-methyl-1H-indole-3-carboxamide **(4e)**: Purified by dissolving the material in acetone, filtering any solid (Pd black), and recrystallizing and washing with MeCN to give the product as brown crystals, (136 mg, 77%). ^{1}H NMR (DMSO-d_6) δ 11.91 (s, 1H), 8.35 (s, 1H), 8.05 – 7.92 (m, 1H), 7.65 – 7.42 (m, 4H), 7.31 – 7.22 (m, 2H), 7.22 – 7.12 (m, 1H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 159.1 (C), 141.5 (C), 136.9 (C), 135.6 (CH), 130.3 (CH), 126.5 (C), 122.8 (CH), 121.9 (CH), 120.8 (CH), 119.4 (CH), 118.8 (CH), 112.7 (CH), 110.8 (CH), 106.5 (C), 55.6 (CH_3), 33.4 (CH_3);

mp: 168 – 170 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_4S$ 345.0909: Found 345.0902; LC purity (254 nm) = >99%.

1-Methyl-N-((2,3,4-trichlorophenyl)sulfonyl)-1H-indole-3-carboxamide **(4g)**: Purified by dissolving the material in acetone, filtering any solid (Pd black), and recrystallizing and washing with MeCN to give the product as opaque white crystals (156 mg, 73%). ^{1}H NMR (DMSO-d_6) δ 12.54 (br s, 1H), 8.50 (s, 1H), 8.18 (d, J = 8.7 Hz, 1H), 7.98 – 7.89 (m, 2H), 7.53 (d, J = 8.2 Hz, 1H), 7.25 (ddd, J = 8.3, 7.2, 1.2 Hz, 1H), 7.16 (ddd, J = 8.0, 7.2, 0.9 Hz, 1H), 3.87 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.5 (C), 138.2 (C), 138.0 (C), 137.0 (C), 136.1 (CH), 132.6 (C), 131.1 (CH), 130.7 (C), 129.2 (CH), 126.5 (C), 123.0 (CH), 122.0 (CH), 120.8 (CH), 110.9 (CH), 105.9 (C), 33.5 (CH_3); mp: 201 – 203 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}Cl_3N_2O_3S$ 416.9634: Found 416.9635; LC purity (254 nm) = 95%.

1-Methyl-N-((3-(trifluoromethyl)phenyl)sulfonyl)-1H-indole-3-carboxamide **(4h)**: Purified by column chromatography (25 to 75% EtOAc in pentane and 0.1% HCOOH) to give the product as beige crystals (156 mg, 86%). ^{1}H NMR (DMSO-d_6) δ 12.14 (br s, 1H), 8.35 (s, 1H), 8.34 – 8.30 (m, 1H), 8.27 (s, 1H), 8.13 – 8.08 (m, 1H), 7.99 – 7.94 (m, 1H), 7.91 (t, J = 7.9 Hz, 1H), 7.53 (d, J = 8.2 Hz, 1H), 7.26 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.18 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 3.85 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.7 (C), 141.5 (C), 137.0 (C), 136.0 (CH), 131.6 (CH), 130.9 (CH), 130.2 (q, J = 3.2 Hz, CH), 130.1 – 129.0 (m, C), 126.4 (C), 124.1 (q, J = 3.9 Hz, CH), 123.4 (q, J = 274.8 Hz, CF_3), 122.9 (CH), 122.0 (CH), 120.7 (CH), 110.9 (CH), 106.2 (C), 33.4 (CH_3); mp: 191 – 193 °C; HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{13}F_3N_2O_3SNa$ 405.0491: Found 405.0490; LC purity (254 nm) = >99%.

N-((4-Cyanophenyl)sulfonyl)-1-methyl-1H-indole-3-carboxamide **(4i)**: Purified by filtering and washing the solid with cold MeCN to give the product as a cream-colored solid (142 mg, 88%). ^{1}H NMR (DMSO-d_6) δ 12.20 (br s, 1H), 8.36 (s, 1H), 8.17 (d, J = 8.2 Hz, 2H), 8.12 (d, J = 8.6

Hz, 2H), 7.99 – 7.92 (m, 1H), 7.56 – 7.50 (m, 1H), 7.26 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.18 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 3.85 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.7 (C), 144.2 (C), 137.0 (C), 136.0 (CH), 133.3 (2×CH), 128.3 (2×CH_3), 126.4 (C), 122.9 (CH), 122.0 (CH), 120.7 (CH), 117.6 (C), 115.7 (C), 110.9 (CH), 106.2 (C), 33.4 (CH_3); HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{13}N_3O_3SNa$ 362.0570: Found 362.0569; LC purity (254 nm) = >99%.

1-Methyl-N-((4-nitrophenyl)sulfonyl)-1H-indole-3-carboxamide **(4j)**: Purified by dissolving the material in minimal DMF, filtering any black solid (Pd black), and precipitating and washing with MeCN to give the product as a yellow solid (155 mg, 79%). ^1H NMR (DMSO-d_6) δ 12.26 (br s, 1H), 8.51 – 8.43 (m, 2H), 8.37 (s, 1H), 8.30 – 8.19 (m, 2H), 7.95 (d, *J* = 7.9 Hz, 1H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.30 – 7.23 (m, 1H), 7.22 – 7.13 (m, 1H), 3.86 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.7 (C), 150.1 (C), 145.5 (C), 137.0 (C), 136.0 (CH), 129.1 (2×CH), 126.4 (C), 124.5 (2×CH), 122.9 (CH), 122.0 (CH), 120.7 (CH), 110.9 (CH), 106.2 (C), 33.4 (CH_3); HRMS (ESI-TOF) m/z: $[M - H]^-$ Calcd for $C_{16}H_{12}N_3O_5S$ 358.0498: Found 358.0503; LC purity (254 nm) = >99%.

N-((4,5-Dichlorothiophen-2-yl)sulfonyl)-1-methyl-1H-indole-3-carboxamide **(4k)**: Purified by column chromatography (75% EtOAc in pentane and 0.1% HCOOH) followed by recrystallization and washing with minimal MeCN to give the product as purple crystals (65 mg, 81%). ^1H NMR (DMSO-d_6) δ 12.44 (br s, 1H), 8.34 (s, 1H), 8.06 (ddd, *J* = 7.8, 1.4, 0.8 Hz, 1H), 7.91 (s, 1H), 7.56 (ddd, *J* = 8.2, 1.0, 0.8 Hz, 1H), 7.29 (ddd, *J* = 8.3, 7.1, 1.4 Hz, 1H), 7.23 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 3.86 (s, 3H); $^{13}C\{1H\}$ NMR (DMSO-d_6) δ 161.9 (C), 138.0 (C), 137.0 (C), 136.1 (CH), 132.0 (CH), 131.2 (C), 126.4 (C), 123.5 (C), 123.0 (CH), 122.1 (CH), 120.8 (CH), 110.9 (CH), 106.2 (C), 33.5 (CH_3); mp,: 168 – 170 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{11}Cl_2N_2O_3S_2$ 388.9588: Found 388.9590; LC purity (254 nm) = >99%.

1-Methyl-N-(thiophen-2-ylsulfonyl)-1H-indole-3-carboxamide **(4l)**: Purified by dissolving the material in acetone and minimal DMF, filtering any solid (Pd black), recrystallizing by slow evaporation of the solution and washing with cold MeCN to give the product as brown crystals, (145 mg, 89%). ^{1}H NMR (DMSO-d_6) δ 12.08 (s, 1H), 8.34 (s, 1H), 8.04 (ddd, J = 7.8, 1.4, 0.8 Hz, 1H), 8.01 (dd, J = 5.0, 1.4 Hz, 1H), 7.85 (dd, J = 3.8, 1.4 Hz, 1H), 7.53 (ddd J = 8.2, 1.0, 0.8 Hz, 1H), 7.27 (ddd, J = 8.2, 7.1, 1.3 Hz, 1H), 7.23 – 7.18 (m, 2H), 3.84 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.6 (C), 140.7 (C), 136.9 (C), 135.6 (CH), 134.1 (CH), 133.8 (CH), 127.3 (CH), 126.5 (C), 122.9 (CH), 121.9 (CH), 120.8 (CH), 110.8 (CH), 106.4 (C), 33.4 (CH_3); mp: 214 – 216 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_3S_2$ 321.0368: Found 321.0368; LC purity (254 nm) = 98%.

1-Methyl-N-((1-methyl-1H-imidazol-4-yl)sulfonyl)-1H-indole-3-carboxamide **(4m)**: Purified by washing the solid with acetone, recrystallizing in DMSO (0.4 mL) and washing the residual solid with DCM to give the product as cream-colored crystals (64 mg, 44%). ^{1}H NMR (DMSO-d_6) δ 11.72 (s, 1H), 8.38 (s, 1H), 8.03 – 7.99 (m, 1H), 7.98 (d, J = 1.4 Hz, 1H), 7.75 (d, J = 1.4 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.25 (ddd, J = 8.3, 7.1, 1.3 Hz, 1H), 7.18 (ddd, J = 8.1, 7.1, 1.1 Hz, 1H), 3.84 (s, 3H), 3.73 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 161.4 (C), 139.3 (CH), 138.6 (C), 136.9 (C), 135.2 (CH), 126.6 (C), 126.5 (CH), 122.7 (CH), 121.7 (CH), 120.9 (CH), 110.7 (CH), 106.8 (C), 33.6 (CH_3), 33.4 (CH_3); mp: 246 – 248 °C; HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{14}N_4O_3SNa$ 341.0679: Found 341.0679; LC purity (254 nm) = >99%.

N-(Isopropylsulfonyl)-1-methyl-1H-indole-3-carboxamide **(4o)**: Purified by dissolving the material in minimal DMF, filtering any black solid (Pd black), and recrystallizing and washing with MeCN to give the product as light-green crystals (110 mg, 73%). ^{1}H NMR (DMSO-d_6) δ 11.37 (s, 1H), 8.38 (s, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.0 Hz, 1H), 7.34 – 7.26 (m, 1H), 7.26 – 7.16 (m, 1H), 3.94 – 3.87 (m, 1H), 3.86 (s, 3H), 1.33 (d, J = 6.9 Hz, 6H); ^{13}C{1H} NMR (DMSO-d_6) δ 162.6 (C), 137.0 (C), 135.5 (CH), 126.7 (C), 122.8 (CH), 121.9 (CH), 120.9

(CH), 110.8 (CH), 106.5 (C), 52.7 (CH), 33.4 (CH_3), 15.6 (2×CH_3); mp: 225 – 227 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}N_2O_3S$ 281.00960: Found 281.0971; LC purity (254 nm) = 97%.

N-(Butylsulfonyl)-1-methyl-1H-indole-3-carboxamide **(4p)**: Purified by dissolving the material in minimal DMF, filtering any black solid (Pd black), and recrystallizing and washing with MeCN to give the product as yellow crystals (100 mg, 70%). ^{1}H NMR (DMSO-d_6) δ 11.45 (s, 1H), 8.36 (s, 1H), 8.14 – 8.07 (m, 1H) , 7.58 – 7.51 (m, 1H) , 7.29 (ddd, J = 8.2, 7.0, 1.4 Hz, 1H), 7.23 (ddd, J = 8.2, 7.0, 1.2 Hz, 1H), 3.86 (s, 3H), 3.57 – 3.46 (m, 2H), 1.69 (p, J = 7.5 Hz, 2H), 1.42 (h, J = 7.4 Hz, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 162.6 (C), 137.0 (C), 135.5 (CH), 126.7 (C), 122.8 (CH), 121.9 (CH), 120.9 (CH), 110.8 (CH), 106.5 (C), 52.4 (CH_2), 33.4 (CH_3), 25.1 (CH_2), 20.7 (CH_2), 13.5 (CH_3); m: 158 – 159 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}N_2O_3S$ 295.1116: Found 295.1117; LC purity (254 nm) = 99%.

Methyl 3-(N-(1-methyl-1H-indole-3-carbonyl)sulfamoyl)propanoate **(4q)**: Purified by diluting the material with 150 mL ether, washing with water (3 × 50 mL), brine, drying with $MgSO_4$ and evaporating the ether to give a cream-colored solid (108 mg, 73%). ^{1}H NMR (DMSO-d_6) δ 11.56 (s, 1H), 8.35 (s, 1H), 8.11 (ddd, J = 7.7, 1.4, 0.7 Hz, 1H), 7.56 (ddd, J = 8.1, 1.0, 0.7 Hz, 1H), 7.29 (ddd, J = 8.2, 7.1, 1.4 Hz, 1H), 7.24 (ddd, J = 8.1, 7.1, 1.2 Hz, 1H), 3.86 (s, 3H), 3.80 (t, J = 7.2 Hz, 2H), 3.58 (s, 3H), 2.81 (t, J = 7.1 Hz, 2H); ^{13}C{1H} NMR (DMSO-d_6) δ 170.5 (C), 162.5 (C), 137.0 (C), 135.6 (CH), 126.6 (C), 122.9 (CH), 121.9 (CH), 120.9 (CH), 110.8 (CH), 106.5 (C), 51.9 (CH_3), 48.4 (CH_2), 33.4 (CH_3), 28.2 (CH_2); HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{16}N_2O_5SNa$ 347.0672: Found 347.0671; LC purity (254 nm) = >99%.

N-(Benzylsulfonyl)-1-methyl-1H-indole-3-carboxamide **(4r)**: Purified by dissolving the material in acetone, filtering any solid (Pd black), and recrystallizing and washing with MeCN

to give the product as small crystals (151 mg, 91%). ^{1}H NMR (DMSO-d_6) δ 11.39 (br s, 1H), 8.28 – 8.13 (m, 2H), 7.55 (d, J = 7.9 Hz, 1H), 7.37 – 7.23 (m, 7H), 4.83 (s, 2H), 3.83 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 163.4 (C), 137.0 (C), 135.3 (CH), 130.7 (2×CH), 129.8 (C), 128.5 (2×CH), 128.3 (CH), 126.8 (C), 122.7 (CH), 121.8 (CH), 121.1 (CH), 110.8 (CH), 107.2 (C), 58.3 (CH_2), 33.4 (CH_3); mp: 211 – 212 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{17}N_2O_3S$ 329.0960: Found 329.0951; LC purity (254 nm) = >99%.

1-Methyl-N-tosyl-1H-pyrrole-2-carboxamide **(6a)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) followed by recrystallization in minimal hot ethanol to give the product as cream-colored crystals (161 mg, 76%). ^{1}H NMR (DMSO-d_6) δ 11.85 (s, 1H), 7.88 – 7.82 (m, 2H), 7.44 – 7.40 (m, 2H), 7.19 (dd, J = 4.1, 1.7 Hz, 1H), 7.07 (t, J = 1.9 Hz, 1H), 6.07 (dd, J = 4.1, 2.5 Hz, 1H), 3.70 (s, 3H), 2.38 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 158.4 (C), 143.9 (C), 137.2 (C), 131.6 (CH), 129.5 (2×CH), 127.6 (2×CH), 122.3 (C), 117.5 (CH), 107.6 (CH), 36.6 (CH_3), 21.1 (CH_3); mp: 167 – 169 °C; HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_{13}H_{14}N_2O_3SNa$ 301.0617: Found 301.0617; LC purity (254 nm) = >99%.

1-Phenyl-N-tosyl-1H-pyrrole-2-carboxamide **(6b)**: Purified by dissolving the material in acetone, filtering any solid (Pd black), recrystallizing by slow evaporation of the MeCN/acetone solution and washing with cold MeCN to give the product as green crystals, (120 mg, 84%). ^{1}H NMR (DMSO-d_6) δ 12.06 (s, 1H), 7.79 – 7.74 (m, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.37 – 7.31 (m, 3H), 7.28 (dd, J = 4.0, 1.7 Hz, 1H), 7.21 (dd, J = 2.6, 1.7 Hz, 1H), 7.15 – 7.07 (m, 2H), 6.29 (dd, J = 4.0, 2.7 Hz, 1H), 2.37 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 157.6 (C), 143.9 (C), 139.7 (C), 136.9 (C), 131.2 (CH), 129.5 (2×CH), 128.6 (2×CH), 127.4 (2×CH), 127.3 (CH), 125.4 (2×CH), 123.5 (C), 118.6 (CH), 109.2 (CH), 21.0 (CH_3); mp: 208 – 209 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{13}N_2O_3S_2$ 341.0960: Found 341.0971; LC purity (254 nm) = >99%.

N-Tosyl-1H-pyrrole-2-carboxamide **(6c)**: Purified by column chromatography (30 to 75% EtOAc in pentane and 0.1% HCOOH) followed by recrystallization in minimal hot ethanol to give the product as white crystals, (177 mg, 77%). ^{1}H NMR (DMSO-d_6) δ 11.96 (s, 1H), 11.72 (s, 1H), 7.91 – 7.82 (m, 2H), 7.45 – 7.39 (m, 2H), 7.13 (ddd, J = 3.9, 2.5, 1.4 Hz, 1H), 7.05 – 6.98 (m, 1H), 6.13 (ddd J = 3.8, 2.5, 2.3 Hz, 1H), 2.38 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 157.9 (C), 144.0 (C), 137.1 (C), 129.4 (2×CH), 127.7 (2×CH), 125.1 (CH), 123.3 (C), 114.9 (CH), 109.6 (CH), 21.1 (CH_3); mp: 209 – 211 °C; HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{13}N_2O_3S$ 265.0647: Found 265.0649; LC purity (254 nm) = >99%.

N-((2-(1H-pyrrol-1-yl)phenyl)carbamoyl)-4-methylbenzenesulfonamide **(6é)**: Purified by column chromatography (30 to 50% EtOAc in pentane and 0.1% HCOOH) to give the product as a cream-colored solid (68.0 mg, 46%). ^{1}H NMR (DMSO-d_6) δ 11.15 (br s, 1H), 7.93 (s, 1H), 7.81 – 7.75 (m, 3H), 7.43 (d, J = 8.1 Hz, 2H), 7.32 (ddd, J = 8.3, 7.1, 2.0 Hz, 1H), 7.25 – 7.14 (m, 2H), 6.84 (t, J = 2.1 Hz, 2H), 6.26 (t, J = 2.1 Hz, 2H), 2.40 (s, 3H); ^{13}C{1H} NMR (DMSO-d_6) δ 149.5 (C), 144.0 (C), 136.8 (C), 132.3 (C), 132.0 (C), 129.6 (2×CH), 127.9 (CH), 127.4 (2×CH), 127.1 (CH), 124.8 (CH), 123.1 (CH), 122.0 (2×CH), 109.8 (2×CH), 21.1 (CH_3); HRMS (ESI-FT ICR) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{17}N_3O_3SNa$ 378.0883: Found 378.0882; LC purity (254 nm) = >99%.

General information radiochemistry

[^{11}C]CO_2 was obtained via the ^{14}N(p,α)^{11}C nuclear reaction utilizing 17 MeV protons (45 μA, 1 μAh, MC-17 cyclotron, Scanditronix) irradiated on a gas target consisting of nitrogen and oxygen gas (0.05%). The formed [^{11}C]CO_2 was transferred in a stream of helium to the unit depicted in Figure S1 where it was converted to [^{11}C]CO and delivered in stream of xenon transfer gas (1.5 mL/min) to the capped reaction vial (3.0-3.8 GBq) containing the reaction mixture.[28,40–43] The gas was bubbled through the mixture until the transfer of the [^{11}C]CO to the vial was complete (10-15 s) and then the transfer needle was removed. High recovery of the poorly soluble [^{11}C]CO was achieved by omitting the vent needle, facilitated by the high solubility of the transfer gas which circumvented significant pressure increase. A radioactivity measurement (A0) was carried out to determine the total amount of [^{11}C]CO introduced (3.4 ± 0.4 GBq). After the carbonylation reaction a radioactivity measurement (A1) was taken to confirm that no gaseous radioactive compound leaked from the vial during the reaction and then the solution and vial was purged with helium gas to remove unreacted [^{11}C]CO and any by-products too volatile to be analyzed by analytical HPLC. Subsequently, a radioactivity measurement (A2) was carried out to assess the amount of [^{11}C]CO that had been converted to non-volatiles. The conversion (%) of [^{11}C]CO was calculated using decay corrected values; *Conversion = A2 / A0 x 100*. The product selectivity (%) was determined from the percentage of desired labelled *N*-acylsulfonamide amide present in the purged solution assessed by analytical HPLC (VWR LaChrom Elite) equipped with an auto-sampler (L-2200), pump (L-2130), diode array detector (L-2450), radiodetector (Flow-Count PMT, Bioscan). Column: Luna C18(2) 3μ 100Å 150x4.6 mm. Eluents: A = ammonium formate (pH 3.5, 50 mM); B = acetonitrile (gradient elution 0-7 min 45-95% B, 7-12 min 95% B, 1 mL/min). The radiochemical yield was calculated from the [^{11}C]CO conversion and the product selectivity; *Radiochemical yield (%) = Conversion x Selectivity / 100*.

Synthesis of 1-methyl-*N*-tosyl-1*H*-indole-3-[^{11}C]carboxamide ([^{11}C]3a):

$Pd_2(dba)_3$ (0.31 mg, 0.34 μmol) and PPh_3 (1.1 mg, 4.1 μmol) were added to an oven-dried 1 mL vial and dissolved in THF (250 μL). *N*-Methylindole (10 mg, 0.76 μmol) and tosyl azide (10 mg, 0.51 μmol) were added, the vial was capped with a Teflon/silicon septum and the mixture was gently degassed with helium under 2 min and then vortexed. After introduction of [^{11}C]CO the vial was heated at 130°C for 5 min. A sample from the reaction mixture was analyzed by analytical HPLC, see representative chromatogram in figure S2. The conversion, selectivity and radiochemical yield were calculated as described above.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at …

Copies of ^{1}H and ^{13}C{1H} NMR spectra and chromatograms for all compounds obtained (PDF)

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Notes

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