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Direct Amidation of Carboxylic Acids with Nitroarenes

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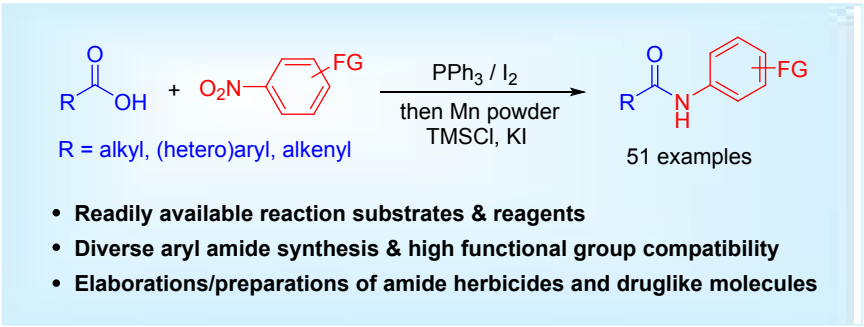


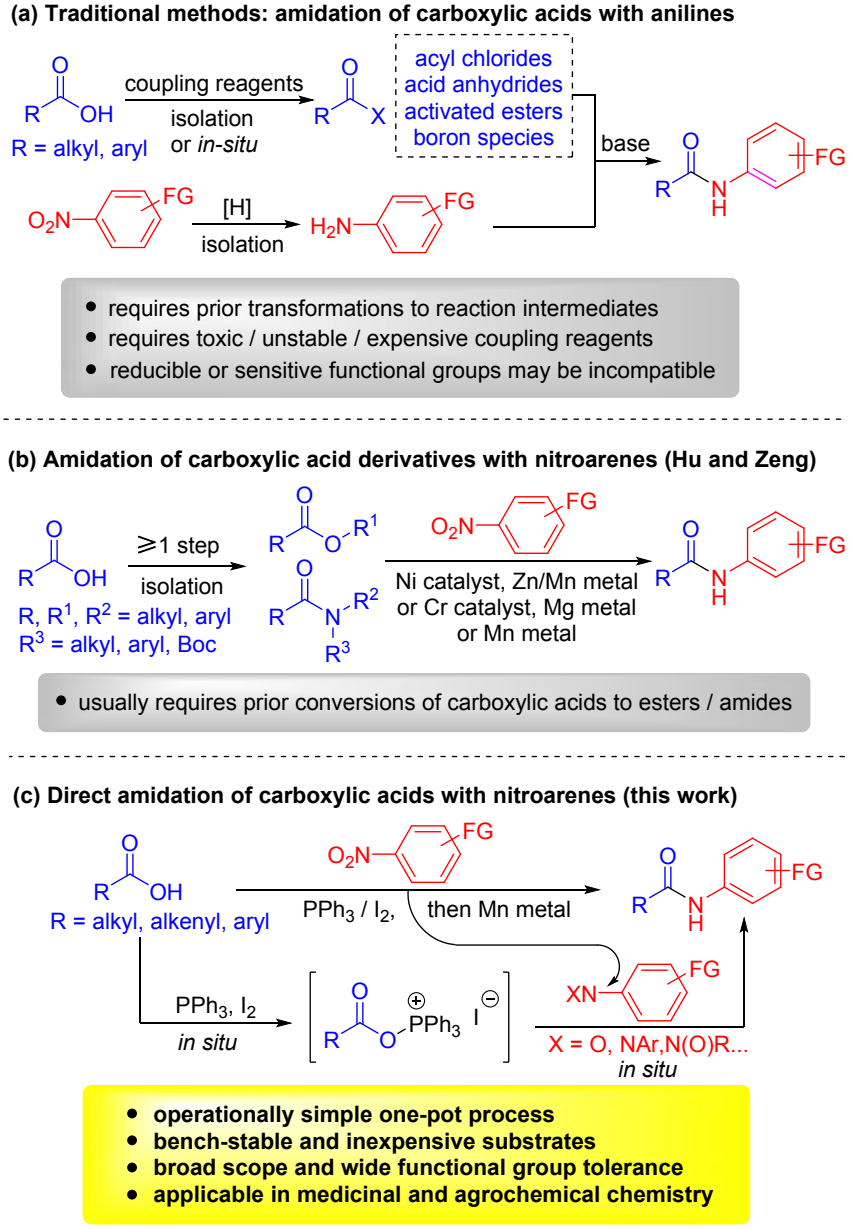
ABSTRACT: *N*-aryl amides are an important class of compounds in pharmaceutical and agrochemical chemistry. Rapid and low-cost synthesis of *N*-aryl amides remains in high demand. Herein, we disclose an operationally simple process to access *N*-aryl amides directly from readily available nitroarenes and carboxylic acids as coupling substrates. This method involves the in-situ activation of carboxylic acids to acyloxyphosphonium salt for one-pot amidation, without the need for isolation of the corresponding synthetic intermediates. Furthermore, the ease of preparation and workup allows the quick and efficient synthesis of a wide range of *N*-aryl amides, including several amide-based druglike and agrochemical molecules

INTRODUCTION

N-Aryl amides[1-3] are ubiquitous structural motifs in many pharmaceuticals,[4,5] agrochemicals,[6] and functional material molecules. Generally, *N*-aryl amides are constructed via the coupling reactions of anilines with carboxylic acids in the presence of stoichiometric activating reagents, such as acid chlorides, acid anhydrides, carbodiimides, and boron compounds (Scheme 1a).[7] However, these activating reagents are usually unstable, toxic, or expensive (Scheme 1a, top). In addition, the pre-activation process could lead to side reactions. On the other hand, anilines are usually prepared beforehand via the tedious metal- and acid-mediated reduction of nitroarenes (Scheme 1a, bottom).[8] Such reduction processes would be incompatible with nitroarenes containing reducible or sensitive functional groups. To overcome these problems, recent research on the amide synthesis has paid more attention to the transition metal-promoted direct chemical transformation of readily available nitroarenes.[9-14] For instance, the groups of Beller,[9] Driver,[10] and Wu[11] described the Pd-catalyzed aminocarbonylation of olefins or arenes with nitroarenes for the synthesis various amides, whereas Hu[12] and Zeng[13] reported the Ni-catalyzed, Cr-catalyzed, or Mn-mediated reductive amidation of nitroarenes with carboxylic acid esters, Boc-protected secondary amides, or tertiary amides (Scheme 1b). In the latter protocols, Zn, Mn, and Mg metals were used as reductants to reduce nitroarenes to more reactive nitrogen-containing intermediates (e.g. nitrosoarenes, *N*-aryl hydroxylamines, azoarenes, and azoxyarenes) for subsequent amidation. These studies have opened an interesting and attractive research area for the development of alternative amidation

methods using nitroarenes as nitrogen sources.[15]

Scheme 1. Synthesis of *N*-aryl amides from carboxylic acid derivatives and nitroarenes.



It is striking, however, that direct transformation of carboxylic acids and nitroarenes into *N*-aryl amides still remains a formidable challenge and such a potentially useful process is hitherto elusive. Robins and co-workers[16a] once reported the utility of

triphenylphosphine (PPh_3) and iodine (I_2) to activate the amide linkages of hypoxanthine nucleosides for further transformations, while Lakshman et al. described the application of PPh_3/I_2 to convert carboxylic acid into reactive acyloxyphosphonium iodide.[16b] Encouraged by these important precedents, we envisioned that direct amidation could be achieved by activating carboxylic acids to acyloxyphosphonium salts in situ using compatible additives, followed by the one-pot amidation with nitroarenes (Scheme 1c). Herein we report the successful implementation of this combination strategy and outline a more general and efficient approach to various *N*-aryl amide derivatives, including several amide-based druglike and agrochemical molecules.

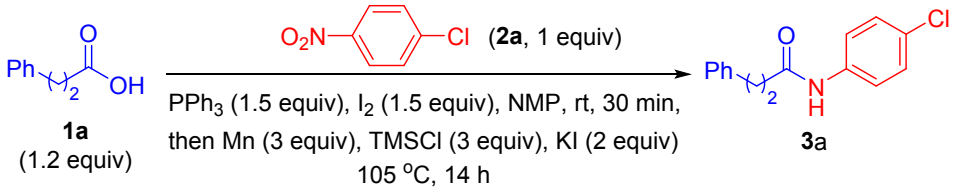
RESULTS AND DISCUSSION

The amidation of hydrocinnamic acid (**1a**) with 1-chloro-4-nitrobenzene (**2a**) was used as the test reaction (Table 1). **1a** (1.2 equiv) was reacted with PPh_3 (1.5 equiv) and I_2 (1.5 equiv) in *N*-methyl-2-pyrrolidinone solvent (NMP) at room temperature in 30 min to form acyloxyphosphonium iodide in situ.[16b] Inspired by Hu's Mn-mediated amidation protocol,[12d,12e] we then added Mn powder (3 equiv) and chlorotrimethylsilane (TMSCl, 3 equiv) in combination with **2a** (1 equiv) and potassium iodide additive (KI, 2 equiv) to proceed the reaction at 105 ^{o}C for 14 h. Gratifyingly, the reaction underwent smoothly to afford the desired *N*-aryl amide product **3a** in 70% yield (entry 1). The use of bromotrimethylsilane (TMSBr) or iodotrimethylsilane (TMSI) in place of TMSCl also furnished the desired product in the

yields of 56% and 62%, respectively (entries 2 and 3). Changing the reaction temperature resulted in relatively lower yields of **3a** (entries 4 and 5). Exploration of other solvents and phosphine / phosphite additives revealed that NMP and PPh_3 were found to be the best choice for this direct amidation process (entries 6–9). The loadings of the additives were next examined, and good yields of amide were obtained when two equivalents of TMSCl or two equivalents of Mn powder was used (entries 10 and 11). Excess phosphine has been used as both deoxygenating reagent and reductant in Cadogan reaction to reduce nitroaromatics for subsequent ring cyclizations.[17] Indeed, the amidation still proceeded in the presence of PPh_3 (4 equiv) even without Mn and TMSCl as reductant and deoxygenating reagent, respectively, delivering the amide in 54% yield (entry 12).

Table 1. **Optimizations of direct amidation of carboxylic acids with nitroarenes.**

Standard conditions:



Entry	Variations from standard conditions[a]	Yield (%)[b]
1	No variation	70
2	TMSBr instead of TMSCl	56
3	TMSI instead of TMSCl	62
4	80 °C instead of 105 °C	52
5	120 °C instead of 105 °C	54

6	DMF instead of NMP	23
7	DMA instead of NMP	43
8	$P(OEt)_3$ instead of PPh_3	15
9	$P(Cy)_3$ instead of PPh_3	31
10	TMSCl (2 equiv) instead of (3 equiv)	57
11	Mn (2 equiv) instead of (3 equiv)	66
12	PPh_3 (4 equiv) instead of (1.5 equiv), and without Mn and TMSCl	54

[a] Optimization was conducted based on the following reaction conditions: **1a** (0.6 mmol), PPh_3 (0.75 mmol), I_2 (0.75 mmol), and NMP (1.5 mL) were stirred at room temperature (rt) for 30 min; then **2a** (0.5 mmol), Mn (1.5 mmol), TMSCl (1.5 mmol), KI (1 mmol), and NMP (1 mL) were added and stirred at 105 °C for 14 h. [b] Isolated yield.

We employed the optimized conditions (Table 1, entry 1) to study the scope of this direct amidation transformation of carboxylic acids with nitroarenes (Figure 1). A wide range of primary, secondary, and tertiary alkyl carboxylic acids were suitable substrates to deliver the desired products **3a**–**3g** in 49–85% yields. In addition, electron-neutral, electron-rich, and electron-deficient aryl-substituted carboxylic acids as well as naphthoic acids reacted smoothly to give the corresponding amides **3h**–**3p** in moderate to good yields. This protocol also allowed the coupling of nitroarenes with heteroaryl carboxylic acids, such as furan (**1q** and **1r**), thiophene (**1s**), and benzothiophene-carboxylic acids (**1t**). Moreover, acrylic acid derivatives, including cinnamic acid (**1u**), *p*-methylcinnamic acid (**1v**), and 2-hexenoic acid (**1w**), were tolerated. The gram-scale synthesis was also allowed by using 7 mmol of nitroarene, affording the amide product **3v** in 74% yield. Furthermore, this sequential one-pot amidation could be simplified to

a single-step process by reacting all substrates and additives simultaneously. Under this single-fraction protocol, **3a**, **3e**, and **3r** could be synthesized in moderate to good yields (42-64%).

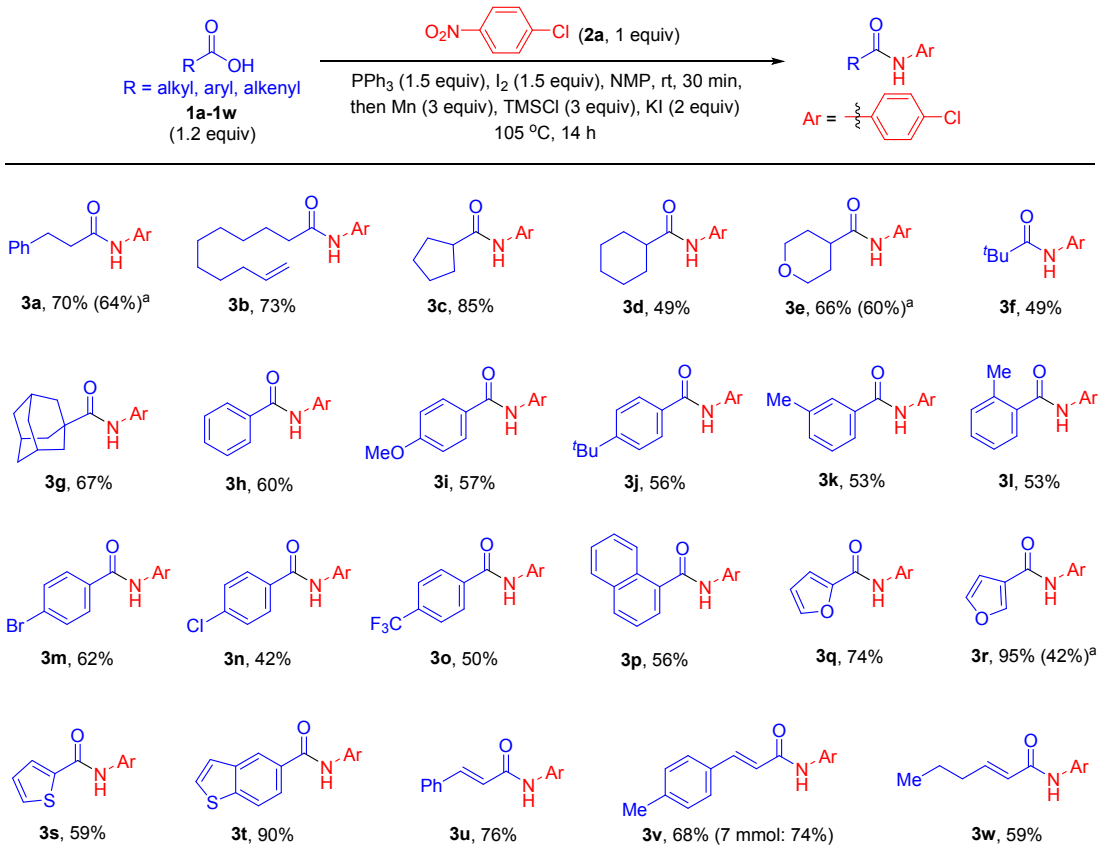


Figure 1. Scope of carboxylic acids in direct amidation with nitroarene. Reaction conditions: **1a-1w** (0.6 mmol), PPh_3 (0.75 mmol), I_2 (0.75 mmol), and NMP (1.5 mL) were stirred at room temperature for 30 min; then **2a** (0.5 mmol), Mn (1.5 mmol), TMSCl (1.5 mmol), KI (1 mmol), and NMP (1 mL) were added and stirred at 105 °C for 14 h. [a] The reaction was performed by reacting all substrates and additives in a single step.

An array of nitroarenes were suitable substrates for reductive amidation with carboxylic acids as well (Figure 2). Electron-neutral and electron-rich nitroarenes were tolerated, giving the corresponding amides **4a**–**4h** in generally good yields. In this context, sterically bulky 2,4-dimethyl-1-nitrobenzene (**2g'**) also reacted smoothly. On the other hand, the amidation of an even more sterically congested 2,6-dimethyl-1-

nitrobenzene was not efficient, giving the amide in less than 20% yield. Electron-deficient nitroarenes could also proceed smoothly to afford the amidation products **4i**–**4o** in good to high yields. Furthermore, nitroheteroarenes containing benzodioxole (**2p'**), benzothiazole (**2q'**), *N*-benzyl indole (**2r'**), and quinoline moieties (**2s'**) were compatible in this protocol. This protocol tolerated a wide range of functional groups in the nitroarene substrates, including dialkylamino (**2b'**), thioether (**2d'**), chloro (**2i'**), fluoro (**2j'**), bromo (**2k'**), trifluoromethyl (**4l'**, **4m'**), cyano (**2n'**), and sulfonamide groups (**2o'**).

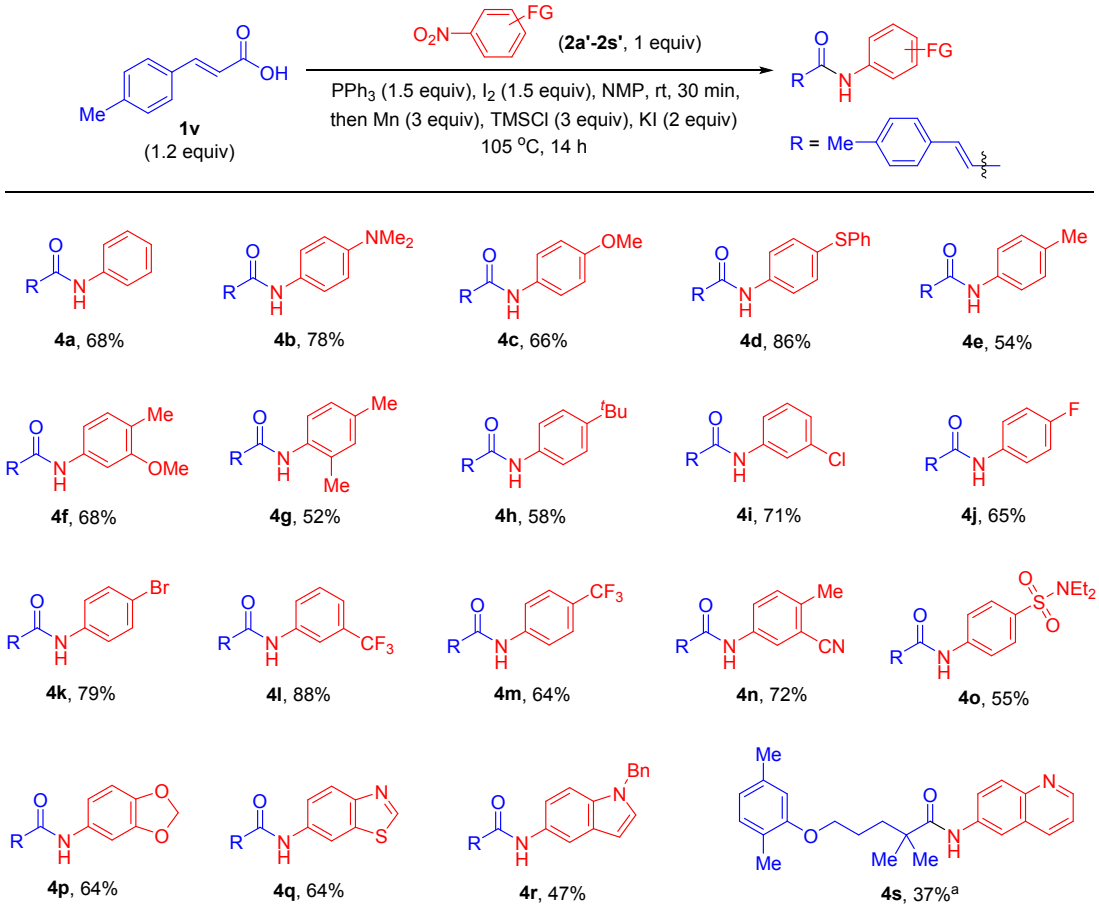


Figure 2. Scope of nitroarenes in direct amidation with carboxylic acid. Reaction conditions: **1v** (0.6 mmol), PPh_3 (0.75 mmol), I_2 (0.75 mmol), and NMP (1.5 mL) were stirred at room temperature for 30 min; then **2a'-2s'** (0.5 mmol), Mn (1.5 mmol), TMSCl (1.5 mmol), KI (1 mmol), and NMP (1 mL) were added and stirred at 105 °C for 14 h. [a] Gemfibrozil was used instead of **1v**.

To illustrate its utility, the present amidation method was applied for the modification of agrochemical and pharmaceutical molecules bearing the carboxylic acid moieties (Figure 3). MCPA, an herbicide, could be transformed to the amide derivative **5a** in 61% yield under this protocol. Moreover, the drug-based carboxylic acids, such as Naproxen, Ibuprofen, Probenecid, Gemfibrozil, dehydrocholic acid, and Bezafibrate, could all undergo this amidation reaction to afford the corresponding drug derivatives **5b**–**5g**. Furthermore, the fungicide Mepronil **5h**[18] was prepared in 83% yield using stable and inexpensive *o*-toluic acid as well as readily available 1-isopropyl-3-nitrobenzene under the current protocol. Likewise, the benzoxazole-bearing antibacterial agent **5i**[19] and the inhibitor of human 11β-HSD1 **5j**[20] could also be synthesized directly from the corresponding carboxylic acids and nitroheteroarenes. In contrast to the traditional methods for synthesis of these bioactive compounds,[18-20] the current transformation could be conducted without the need for isolation or purification of any synthetic intermediates.

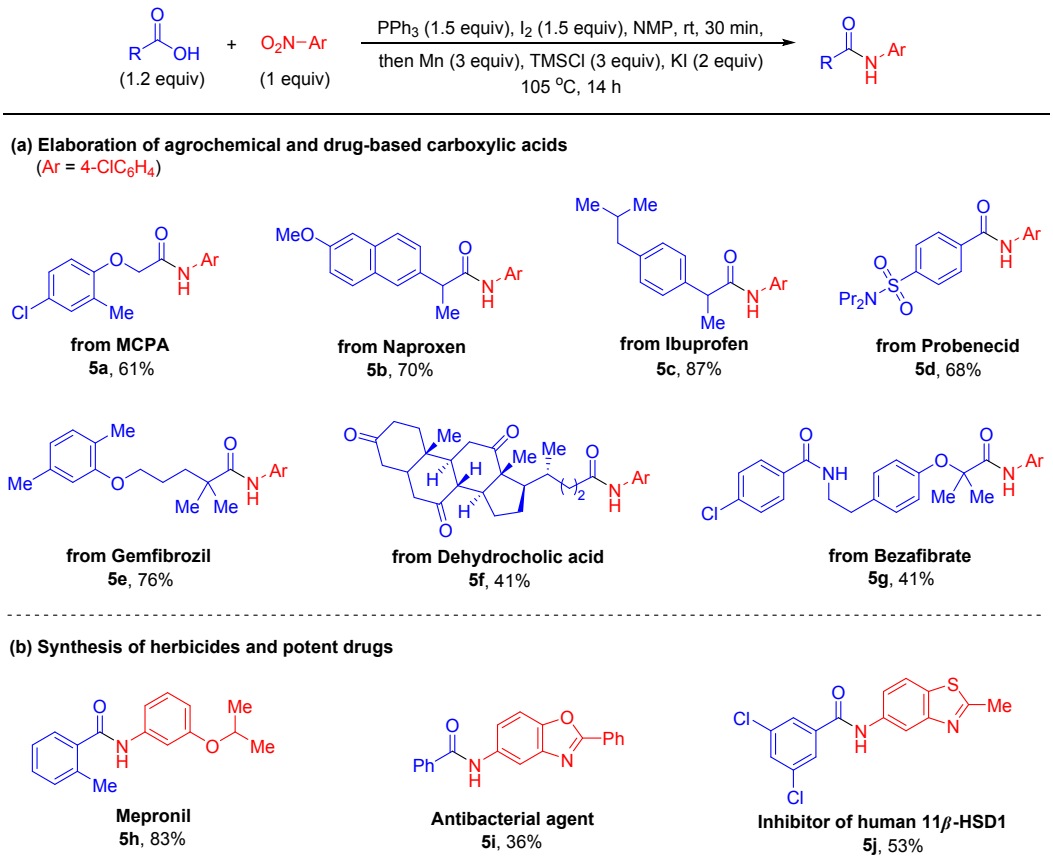


Figure 3. Synthetic utility of the direction amidation in agrochemical and medicinal chemistry.

During the amidation process, nitroarenes could be converted to nitrosoarenes, *N*-aryl hydroxylamines, azoarenes, azoxyarenes, 1,2-diaryl hydrazines, and anilines under the reductive conditions.[12,14b,21] To probe the roles of these nitrogen-containing species as intermediates in this amidation transformation, the reactions of these species with carboxylic acid under the conditions relevant to the amidation were monitored (Figure 4a). While 4-methylcinnamic acid **1v** reacted with nitrobenzene to give *N*-phenyl 4-methylcinnamate **4a** in 68% yield (Figure 2), the condensation of nitrosobenzene **6a** or *N*-phenyl hydroxylamine **6b** with **1v** under otherwise identical conditions proceeded to afford **4a** in 36% and 39% isolated yields, respectively. Thus, nitrosobenzene and *N*-phenyl hydroxylamine are most likely the active intermediates for this amidation

reaction. The diminishment of yields with *N*-containing intermediates could be attributed to the difference in effective concentration of substrates or additives compared with the parent reaction. TMSCl is essential in the amidation with nitrosobenzene or *N*-phenyl hydroxylamine, as only low yields of the amide product were formed (6–16%) when TMSCl was omitted. On the other hand, azobenzene **6c** only reacted with 4-methylcinnamic acid to give the amide in 14% yield, while azoxybenzene **6d**, 1,2-diphenyl hydrazine **6e**, and aniline **6f** reacted to give a trace of amides, suggesting that they are unlikely the intermediates for amidation.

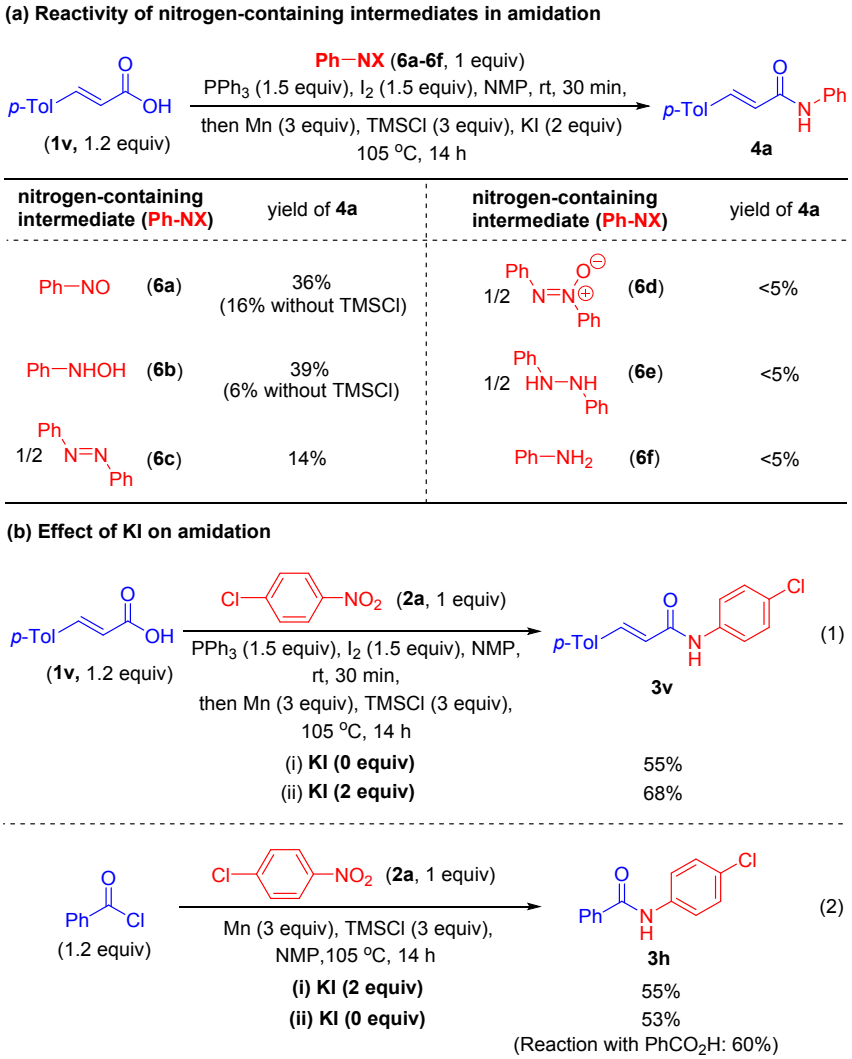


Figure 4. Mechanistic study on the direct amidation of carboxylic acids with nitroarenes.

KI is essential in promoting the efficiency of amidation. When KI was omitted, 4-methylcinnamic acid **1v** reacted with 1-chloro-4-nitrobenzene **2a** to form the amide **3v** in 55% yield [Figure 4b, eq (1), (i)]. When KI was added, the yield of **3v** could be promoted to 68% yield [Figure 4b, eq (1), (ii)]. The results suggested that the in-situ formed acyloxyphosphonium iodide itself is sufficiently reactive for amidation, while the additional iodide probably aids in partially converting acyloxyphosphonium iodide to more reactive acyl iodide to further promote the amidation process. Moreover, benzoyl iodide, which was formed via the in-situ substitution of benzoyl chloride with KI, and benzoyl chloride itself underwent amidation smoothly under the otherwise identical conditions to give the amide **3h** in 55% and 53% yields, respectively [Figure 4b, eq (2), (i) and (ii)]. The results implied that both acyl iodide and acyl chloride are the viable reaction intermediate in this amidation protocol.

Based on the above results and the analogous reaction mechanisms,[12d,12e] we proposed the mechanism of the reductive amidation of carboxylic acids with nitroarenes. Carboxylic acid is activated by PPh_3 and I_2 to form acyloxyphosphonium iodide[16b] and hydrogen iodide, which is then neutralized by the basic NMP solvent [Figure 5, (i)]. Acyloxyphosphonium iodide can partially react with KI[16b] and TMSCl to form acyl iodide and acyl chloride, respectively, and both of them are also interconvertible [Figure 5, (i)]. TMSCl can also react with KI to form a more reactive TMSI [Figure 5, (ii)]. Meanwhile, nitroarene is reduced by Mn in the presence of TMSCl or TMSI to form nitrosoarene and *N*-aryl hydroxylamine as the most probable nitrogen-containing

intermediates [Figure 5, (iii)]. TMSCl and TMSI likely react as deoxygenating reagents[12] to promote the reduction of nitroarene to nitrosoarene. Nitrosoarene is then further reduced to form *N*-aryl hydroxylamine, and hydrogen iodide (NMP-H^+I^-) generated from the activation of carboxylic acid likely behaves as the proton source to facilitate this process. Finally, nitrosoarene presumably reacts with acyloxyphosphonium iodide, acyl iodide, and acyl chloride in the presence of Mn and TMSCl/TMSI to form a *N*-(trimethylsilyl)oxy amide species **A**,[22] presumably via the oxidative addition of acyloxyphosphonium iodide and acyl halides to Mn to form acyl-Mn species[23] [Figure 5, (iv)]. *N*-Aryl hydroxylamine also presumably reacts with acyloxyphosphonium iodide and acyl halides to form *N*-hydroxy amide species **B**[24] [Figure 5, (iv)]. Both species **A** and **B** further undergo reduction to form amide anion **C**. During the workup process with aqueous acid solution, the amide anion **C** is protonated to furnish *N*-aryl amide. The detailed mechanism of this amidation transformation, especially the bond activation processes mediated by the Mn metal, will be subjected to a further dedicated study.

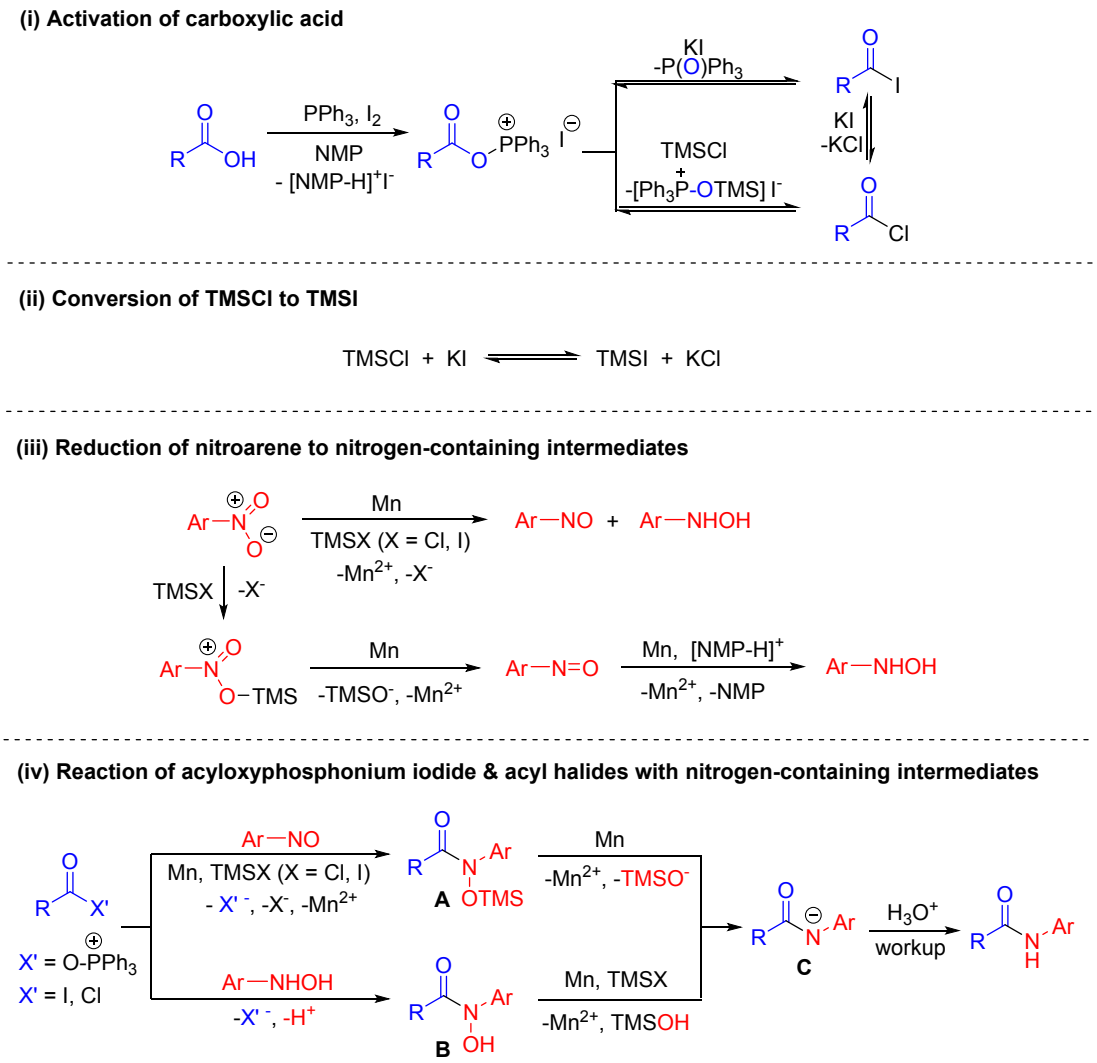


Figure 5. Proposed mechanism of direct amidation of carboxylic acids with nitroarenes.

In conclusion, we have developed a one-pot and streamlined method for direct amidation of carboxylic acids with nitroarenes. Bench-stable and readily available substrates could be employed to afford a wide variety of *N*-aryl amides. A rapid derivatization of agrochemical and drug molecules bearing the carboxylic acid moieties, as well as the expedient synthesis of amide-based agrochemical and druglike molecules, are also demonstrated. This operationally simple protocol also provides a complement to the existing approaches in amide synthesis and would find widespread use in various

industry settings.

EXPERIMENTAL SECTION

General information.

Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance III HD 400 MHz instruments at ambient temperature. All ^{1}H NMR spectra were measured in part per million (ppm, δ) relative to the signal of tetramethylsilane (TMS, 0.00 ppm), the signal of deuterated chloroform ($CDCl_3$, 7.26 ppm), or the signal of residual dimethyl sulfoxide in dimethyl-d_6 sulfoxide (DMSO-d_6, 2.50 ppm).[25] Data for ^{1}H NMR were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant, and integration. All ^{13}C NMR spectra were reported in ppm relative to $CDCl_3$ (77.16 ppm) or DMSO-d_6 (39.52 ppm) and were obtained with complete ^{1}H decoupling.[25] High-resolution mass spectrometry (HRMS) images were obtained on a microTOF-QII or Waters Micromass GCT Premier Instrument.

Unless otherwise noted, all chemicals were used as received without further purifications. 1-Methyl-2-pyrrolidinone (NMP, 99% purity) were dried with 4Å molecular sieve beads prior to use. Manganese powder (Mn), triphenylphosphine (PPh_3), and potassium iodide (KI) were in 99.9%, 98%, and 99% purities. Respectively, chlorotrimethylsilane (TMSCl, 98% purity) was stored in the refrigerator (4 ^{o}C) prior to use. Nitroarenes, including *N*,*N*-diethyl-4-nitrobenzene-sulfonamide,[26] (4-nitrophenyl)(phenyl)sulfane,[27] 1-benzyl-5-nitro-1*H*-indole,[28] 1-isopropoxy-3-

nitrobenzene,[29] and 2-methyl-5-nitrobenzo[*d*]thiazole,[30] were prepared according to the literature procedures.

Flash column chromatography was performed using silica gel (200-300 mesh). The eluents used for column chromatography were presented as ratios of solvent volumes. Yields reported in the publication are isolated yields unless otherwise noted. All new amide products were characterized by ^{1}H and ^{13}C NMR spectroscopies and high-resolution mass spectrometry (HRMS). All known amide products were characterized by ^{1}H and ^{13}C NMR spectroscopies and the spectra were compared with the reported data.

General Procedure for the Amide Synthesis via Sequential One-pot Manganese-Mediated Direct Amidation of Carboxylic Acids with Nitroarenes (General Procedure A). An oven-dried 20 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar was sequentially charged with carboxylic acid (1.2 equiv, 0.60 mmol), triphenylphosphine (PPh_3, 1.5 equiv, 0.75 mmol, 196.7 mg), iodine (I_2, 1.5 equiv, 0.75 mmol, 190 mg), and 1-methyl-2-pyrrolidinone solvent (NMP, 1.5 mL). The tube was capped with an airtight rubber septum, and the tube was degassed in *vacuo* and then backfilled with argon gas for three times. A plastic balloon filled with argon gas was added on the side arm opening of the Schlenk tube, and the resulting mixture was stirred at room temperature for 30 min under the positive argon pressure. At this point, nitroarene (1.0 equiv, 0.50 mmol), manganese powder (Mn, 3.0 equiv, 1.5 mmol, 82 mg), potassium iodide (KI, 2.0 equiv, 166 mg), and chlorotrimethylsilane (TMSCl, 3.0 equiv, 1.5 mmol, 191 μL) followed by NMP solvent (~1.0 mL, to wash away the

chemicals attached on the inner wall) were then quickly transferred into the reaction mixture under a positive balloon argon pressure. The resulting mixture was stirred at 105 °C in a preheated oil bath for 14 h. After the reaction, the reaction mixture was cooled down to room temperature. The reaction mixture was quenched with water (~10 mL) and the aqueous phase was extracted three times with ethyl acetate (EtOAc, ~3×20 mL). The combined organic fraction was further acidified with HCl solution (~1 M (aq), ~20 mL), neutralized with saturated $NaHCO_3$ solution (~30 mL), washed with saturated NaCl solution, dried with anhydrous Na_2SO_4, and then concentrated in *vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography using a solvent mixture (petroleum ether, EtOAc) as an eluent to give the purified amide product.

General Procedure for the Amide Synthesis via Single-step Manganese-Mediated Direct Amidation of Carboxylic Acids with Nitroarenes (General Procedure B). An oven-dried 20 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar was charged with carboxylic acid (1.2 equiv, 0.60 mmol), triphenylphosphine (PPh_3, 1.5 equiv, 0.75 mmol, 197 mg), iodine (I_2, 1.5 equiv, 0.75 mmol, 190 mg), nitroarene (1.0 equiv, 0.50 mmol), manganese powder (Mn, 3.0 equiv, 1.5 mmol, 82 mg), and potassium iodide (KI, 2.0 equiv, 1.0 mmol, 166 mg). The tube was capped with an airtight rubber septum, and the tube was degassed in *vacuo* and then backfilled with argon gas for three times. 1-Methyl-2-pyrrolidinone solvent (2.5 mL) followed by chlorotrimethylsilane (TMSCl, 3.0 equiv, 1.5 mmol, 191 μL) were then quickly

transferred into the reaction mixture under a positive balloon argon pressure. After the addition, a plastic balloon filled with argon gas was added on the side arm opening of the Schlenk tube. The resulting mixture was stirred at 105 ^{o}C in a preheated oil bath for 14 h. After the reaction, the reaction mixture was cooled down to room temperature. The reaction mixture was quenched with water (~10 mL) and the aqueous phase was extracted three times with ethyl acetate (EtOAc, ~3×20 mL). The combined organic fraction was further acidified with HCl solution (~1 M (aq), ~20 mL), neutralized with saturated $NaHCO_3$ solution (~30 mL), washed with saturated NaCl solution, dried with anhydrous Na_2SO_4, and then concentrated in *vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography using a solvent mixture (petroleum ether, EtOAc) as an eluent to give the purified amide product.

***N*-(4-chlorophenyl)-3-phenylpropanamide (3a).[31]**

(i) One-pot, Two-step Reaction: Following the general procedure A, the title compound was prepared using hydrocinnamic acid (1.2 equiv, 0.60 mmol, 90.1 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (9:1) as an eluent to give the title compound as an off-white amorphous solid (90 mg, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.37 (d, J = 8.3 Hz, 2H), 7.33-7.27 (m, 2H), 7.23 (t, J = 8.2 Hz, 5H), 7.16 (s, 1H), 3.04 (t, J = 7.5 Hz, 2H), 2.65 (t, J = 7.5 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 170.5, 140.5, 136.3, 129.3, 129.0, 128.7, 128.4, 126.5, 121.2, 39.4, 31.5.

(ii) Single-step Reaction: Following the general procedure B, the title compound

was isolated in 64% yield (84 mg).

***N*-(4-chlorophenyl)undec-10-enamide (3b)**. Following the general procedure A, the title compound was prepared using undec-10-enoic acid (1.2 equiv, 0.60 mmol, 110.6 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (16:1) as an eluent to give the title compound as a white amorphous solid (106.7 mg, 73%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52-7.42 (m, 3H), 7.26 (d, J = 7.7 Hz, 2H), 5.81 (dq, J = 12.0, 7.0 Hz, 1H), 4.98 (d, J = 27.4 Hz, 1H), 4.94 (d, J = 20.5 Hz, 1H), 2.34 (t, J = 7.4 Hz, 2H), 2.03 (q, J = 6.7 Hz, 2H), 1.77-1.63 (m, 2H), 1.44-1.24 (m, 10H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 171.6, 139.2, 136.5, 129.1, 129.0, 121.1, 114.2, 37.8, 33.8, 29.3, 29.3, 29.1, 28.9, 25.6. (14 carbon signals were observed out of expected 15 carbon signals). **HRMS** (electrospray ionization (ESI)): *m/z* Calc. for $C_{17}H_{25}NOCl$ $[M+H]^+$: 294.1625; Found: 294.1628.

***N*-(4-chlorophenyl)cyclopentanecarboxamide (3c)**. Following the general procedure A, the title compound was prepared using cyclopentanecarboxylic acid (1.2 equiv, 0.60 mmol, 68.5 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (14:1) as an eluent to give the title compound as a white amorphous solid (95.1 mg, 85%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.3 Hz, 2H), 7.34 (s, 1H), 7.26 (d, J = 7.9 Hz, 2H), 2.67 (p, J = 8.0 Hz, 1H), 1.99-1.84 (m, 4H), 1.82-1.72 (m, 2H), 1.67-1.55 (m, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 174.7, 136.7, 129.0, 121.0, 46.8, 30.6, 26.0. (7 carbon signals were observed out of expected

8 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{12}H_{15}NOCl$ $[M+H]^+$: 224.0842; Found: 224.0842.

***N*-(4-chlorophenyl)cyclohexanecarboxamide (3d)**.[32] Following the general procedure A, the title compound was prepared using cyclohexanecarboxylic acid (1.2 equiv, 0.60 mmol, 76.9 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (15:1) as an eluent to give the title compound as a white amorphous solid (57.7 mg, 49%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.14 (s, 1H), 2.22 (t, J = 11.7 Hz, 1H), 1.95 (d, J = 12.5 Hz, 2H), 1.84 (d, J = 11.0 Hz, 2H), 1.72 (s, 1H), 1.53 (dd, J = 22.5, 10.6 Hz, 2H), 1.37-1.17 (m, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 174.3, 136.6, 129.0, 120.9, 46.6, 29.6, 25.6. (7 carbon signals were observed out of expected 9 carbon signals).

***N*-(4-chlorophenyl)tetrahydro-2*H*-pyran-4-carboxamide (3e)**.

(i) One-pot, two-step Reaction: Following the general procedure A, the title compound was prepared using tetrahydro-2*H*-pyran-4-carboxylic acid (1.2 equiv, 0.60 mmol, 78.1 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (2:1) as an eluent to give the title compound as a white amorphous solid (78.9 mg, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 9.6 Hz, 2H), 4.07 (d, J = 11.4 Hz, 2H), 3.45 (t, J = 11.5 Hz, 2H), 2.50 (td, J = 11.2, 5.6 Hz, 1H), 2.00-1.77 (m, 4H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 172.5, 136.3, 129.4, 129.1, 121.1, 67.1, 43.3, 29.2. **HRMS** (ESI): *m/z* Calc. for

$C_{12}H_{15}NO_2Cl$ $[M+H]^+$: 240.0791; Found: 240.0793.

(ii) Single-step Reaction: Following the general procedure B, the title compound was isolated in 60% yield (73 mg).

***N*-(4-chlorophenyl)pivalamide (3f)**.[33] Following the general procedure A, the title compound was prepared using pivalic acid (1.2 equiv, 0.60 mmol, 61.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (18:1) as an eluent to give the title compound as a white amorphous solid (51.8 mg, 49%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49 (d, J = 8.2 Hz, 2H), 7.32 (s, 1H), 7.28 (d, J = 8.9 Hz, 2H), 1.31 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 176.6, 136.6, 129.1, 129.0, 121.2, 39.7, 27.6.

***N*-(4-chlorophenyl)adamantane-1-carboxamide (3g)**.[34] Following the general procedure A, the title compound was prepared using adamantane-1-carboxylic acid (1.2 equiv, 0.60 mmol, 108.2 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (25:1) as an eluent to give the title compound as a white amorphous solid (97.5 mg, 67%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.49 (d, J = 8.3 Hz, 2H), 7.34-7.17 (m, 3H), 2.11 (s, 3H), 1.96 (s, 6H), 1.84-1.68 (m, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 176.1, 136.6, 129.0, 128.9, 121.2, 41.5, 39.3, 38.6, 36.4, 28.1, 27.8.

***N*-(4-chlorophenyl)benzamide (3h)**.[35] Following the general procedure A, the title

compound was prepared using benzoic acid (1.2 equiv, 0.60 mmol, 73.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (15:1) as an eluent to give the title compound as a white amorphous solid (68.9 mg, 60%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.5 Hz, 2H), 7.82 (s, 1H), 7.61 (d, J = 8.5 Hz, 2H), 7.56 (d, J = 7.0 Hz, 1H), 7.50 (t, J = 7.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 165.7, 136.5, 134.6, 132.1, 129.6, 129.2, 128.9, 127.0, 121.4.

***N*-(4-chlorophenyl)-4-methoxybenzamide (3i)**.[36] Following the general procedure A, the title compound was prepared using 4-methoxybenzoic acid (1.2 equiv, 0.60 mmol, 91.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (8:1) as an eluent to give the title compound as a white amorphous solid (74.7 mg, 57%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.5 Hz, 2H), 7.72 (s, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.5 Hz, 2H), 6.98 (d, J = 8.5 Hz, 2H), 3.88 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 165.1, 162.6, 136.7, 129.3, 129.1, 128.9, 126.7, 121.3, 114.1, 55.5.

4-(*tert*-butyl)-*N*-(4-chlorophenyl)benzamide (3j).[37] Following the general procedure A, the title compound was prepared using 4-(*tert*-butyl)benzoic acid (1.2 equiv, 0.60 mmol, 106.9 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (20:1) as an eluent to give the title compound as a white amorphous solid (79.9 mg, 56%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.86-7.75 (m, 3H),

7.60 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 7.7 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 1.35 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 165.6, 155.7, 136.6, 131.7, 129.4, 129.1, 126.9, 125.8, 121.3, 35.0, 31.2.

***N*-(4-chlorophenyl)-3-methylbenzamide (3k)**.[38] Following the general procedure A, the title compound was prepared using 3-methylbenzoic acid (1.2 equiv, 0.60 mmol, 81.7 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (15:1) as an eluent to give the title compound as a white amorphous solid (64.8 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.68 (s, 1H), 7.66-7.56 (m, 3H), 7.38 (d, J = 4.3 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 2.43 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 165.9, 138.8, 136.6, 134.6, 132.8, 129.5, 129.1, 128.7, 127.8, 124.0, 121.4, 21.4.

***N*-(4-chlorophenyl)-2-methylbenzamide (3l)**.[39] Following the general procedure A, the title compound was prepared using 2-methylbenzoic acid (1.2 equiv, 0.60 mmol, 81.7 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (15:1) as an eluent to give the title compound as a white amorphous solid (64.7 mg, 53%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.58 (d, J = 8.1 Hz, 2H), 7.48 (d, J = 7.1 Hz, 2H), 7.42-7.31 (m, 3H), 7.30-7.25 (m, 2H), 2.50 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 168.1, 136.6, 136.0, 131.4, 130.5, 129.5, 129.1, 126.6, 126.0, 121.1, 19.9.

4-bromo-*N*-(4-chlorophenyl)benzamide (3m).[40] Following the general procedure A, the title compound was prepared using 4-bromobenzoic acid (1.2 equiv, 0.60 mmol, 120.6 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (18:1) as an eluent to give the title compound as a white amorphous solid (95.5 mg, 62%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80-7.70 (m, 3H), 7.64 (d, J = 7.7 Hz, 2H), 7.59 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.7, 136.2, 133.4, 132.2, 129.9, 129.2, 128.6, 126.9, 121.5.

4-chloro-*N*-(4-chlorophenyl)benzamide (3n).[41] Following the general procedure A, the title compound was prepared using 4-chlorobenzoic acid (1.2 equiv, 0.60 mmol, 94.0 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (14:1) as an eluent to give the title compound as a white amorphous solid (54.9 mg, 42%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.8 Hz, 2H), 7.77 (s, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.47 (d, J = 7.6 Hz, 2H), 7.34 (d, J = 7.8 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.6, 138.4, 136.2, 133.0, 129.8, 129.2, 129.2, 128.5, 121.5.

***N*-(4-chlorophenyl)-4-(trifluoromethyl)benzamide (3o)**. Following the general procedure A, the title compound was prepared using 4-(trifluoromethyl)benzoic acid (1.2 equiv, 0.60 mmol, 114.1 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (18:1) as an eluent to give the title compound

as a white amorphous solid (75.2 mg, 50%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.98 (d, J = 7.9 Hz, 2H), 7.82 (s, 1H), 7.77 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.4, 137.9, 136.0, 133.8 (d, $^2J_{CF}$ = 32.9 Hz), 130.1, 129.3, 127.5, 126.0 (d, $^3J_{CF}$ = 3.75 Hz), 123.5 (d, $^1J_{CF}$ = 272.3 Hz), 121.6. **HRMS** (ESI): *m/z* Calc. for $C_{14}H_{10}ClF_3NO$ $[M+H]^+$: 300.0403; Found: 300.0410.

***N*-(4-chlorophenyl)-1-naphthamide (3p)**.[42] Following the general procedure A, the title compound was prepared using 1-naphthoic acid (1.2 equiv, 0.60 mmol, 103.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (14:1) as an eluent to give the title compound as a white amorphous solid (78.2 mg, 56%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.33 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.91 (d, J = 7.4 Hz, 1H), 7.76 (s, 1H), 7.72 (d, J = 6.9 Hz, 1H), 7.64 (d, J = 8.1 Hz, 2H), 7.57 (p, J = 7.1 Hz, 2H), 7.49 (t, J = 7.6 Hz, 1H), 7.35 (d, J = 8.1 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 167.5, 136.6, 134.1, 133.8, 131.3, 130.0, 129.7, 129.2, 128.5, 127.5, 126.7, 125.2, 124.7, 121.2. (14 carbon signals were observed out of expected 15 carbon signals).

***N*-(4-chlorophenyl)furan-2-carboxamide (3q)**. Following the general procedure A, the title compound was prepared using furan-2-carboxylic acid (1.2 equiv, 0.60 mmol, 67.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (9:1) as an eluent to give the title compound as a pale yellow amorphous

solid (81.5 mg, 74%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.61 (d, J = 8.3 Hz, 2H), 7.53 (s, 1H), 7.33 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 4.4 Hz, 2H), 6.59-6.56 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 156.0, 147.6, 144.3, 136.0, 129.5, 129.2, 121.1, 115.6, 112.8. **HRMS** (ESI): *m/z* Calc. for $C_{11}H_9NO_2Cl$ $[M+H]^+$: 222.0322; Found: 222.0325.

***N*-(4-chlorophenyl)furan-3-carboxamide (3r)**.

(i) One-pot, Two-step Reaction: Following the general procedure A, the title compound was prepared using furan-3-carboxylic acid (1.2 equiv, 0.60 mmol, 67.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (10:1) as an eluent to give the title compound as a white amorphous solid (104.9 mg, 95%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.54 (d, J = 8.3 Hz, 2H), 7.49 (s, 2H), 7.31 (d, J = 8.3 Hz, 2H), 6.71 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 160.6, 145.2, 144.2, 136.1, 129.6, 129.1, 122.8, 121.5, 108.2. **HRMS** (ESI): *m/z* Calc. for $C_{11}H_9NO_2Cl$ $[M+H]^+$: 222.0322; Found: 222.0325.

(ii) Single-step Reaction: Following the general procedure B, the title compound was isolated in 42% yield (47 mg).

***N*-(4-chlorophenyl)thiophene-2-carboxamide (3s)**. Following the general procedure A, the title compound was prepared using thiophene-2-carboxylic acid (1.2 equiv, 0.60 mmol, 76.9 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (9:1) as an eluent to give the title compound as a pale yellow

amorphous solid (70.2 mg, 59%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.63 (d, J = 2.6 Hz, 1H), 7.57 (m, J = 8.7 Hz, 3H), 7.32 (d, J = 8.4 Hz, 2H), 7.13 (t, J = 4.1 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 159.9, 138.8, 136.2, 131.1, 129.7, 129.2, 128.6, 127.9, 121.4. **HRMS** (ESI): *m/z* Calc. for $C_{11}H_9NOSCl$ $[M+H]^+$: 238.0093; Found: 238.0092.

***N*-(4-chlorophenyl)benzo[*b*]thiophene-5-carboxamide (3t)**. Following the general procedure A, the title compound was prepared using benzo[*b*]thiophene-5-carboxylic acid (1.2 equiv, 0.60 mmol, 106.9 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (10:1) as an eluent to give the title compound as a white amorphous solid (129.9 mg, 90%). **^{1}H NMR** (400 MHz, DMSO-d_6): δ 10.62 (s, 1H), 8.36 (s, 1H), 8.06 (d, J = 7.5 Hz, 1H), 8.02 (d, J = 7.6 Hz, 1H), 7.81 (d, J = 8.5 Hz, 2H), 7.49 (m, 2H), 7.44 (d, J = 8.6 Hz, 2H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6): δ 160.9, 141.0, 140.1, 139.5, 138.1, 129.2, 128.1, 127.1, 126.5, 125.9, 125.6, 123.4, 122.3. **HRMS** (ESI): *m/z* Calc. for $C_{15}H_{11}NOSCl$ $[M+H]^+$: 288.0250; Found: 288.0248.

***N*-(4-chlorophenyl)cinnamamide (3u).**[43] Following the general procedure A, the title compound was prepared using cinnamic acid (1.2 equiv, 0.60 mmol, 88.9 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (11:1) as an eluent to give the title compound as a white amorphous solid (97.4 mg, 76%).**^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.76 (d, J = 15.5 Hz, 1H), 7.58 (d, J = 7.7 Hz,

2H), 7.51 (s, 2H), 7.47 (s, 1H), 7.38 (s, 3H), 7.31 (d, J = 7.9 Hz, 2H), 6.54 (d, J = 15.4 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.0, 142.9, 136.6, 134.5, 130.2, 129.1, 128.9, 128.0, 121.2, 120.4. (10 carbon signals were observed out of expected 11 carbon signals).

(*E*)-*N*-(4-chlorophenyl)-3-(*p*-tolyl)acrylamide (3v).[44]

(i) 0.5 mmol Scale: Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (12:1) as an eluent to give the title compound as a pale yellow amorphous solid (92.5 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, J = 15.5 Hz, 1H), 7.58 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 7.8 Hz, 3H), 7.30 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 7.6 Hz, 2H), 6.49 (d, J = 15.4 Hz, 1H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.2, 142.9, 140.6, 136.7, 131.7, 129.7, 129.3, 129.1, 128.0, 121.1, 119.3, 21.5.

(ii) 7 mmol Scale: Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 8.4 mmol, 1362.4 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 7.0 mmol, 1102.9 mg) using petroleum ether/EtOAc (10:1) as an eluent to give the title compound as a pale yellow amorphous solid (1.41 g, 74%).

(*E*)-*N*-(4-chlorophenyl)hex-2-enamide (3w). Following the general procedure A, the title compound was prepared using (*E*)-hex-2-enoic acid (1.2 equiv, 0.60 mmol, 68.5

mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (18:1) as an eluent to give the title compound as a white amorphous solid (65.5 mg, 59%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52 (d, J = 7.8 Hz, 2H), 7.35 (s, 1H), 7.28 (d, J = 8.5 Hz, 2H), 7.04-6.93 (m, 1H), 5.91 (d, J = 15.1 Hz, 1H), 2.20 (q, J = 7.0 Hz, 2H), 1.56-1.44 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.2, 147.0, 136.6, 129.2, 129.0, 123.7, 121.1, 34.2, 21.4, 13.7. **HRMS** (ESI): *m/z* Calc. for $C_{12}H_{15}NOCl$ $[M+H]^+$: 224.0842; Found: 224.0842.

(*E*)-*N*-phenyl-3-(*p*-tolyl)acrylamide (4a). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and nitrobenzene (1.0 equiv, 0.50 mmol, 61.6 mg) using petroleum ether/EtOAc (9:1) as an eluent to give the title compound as a white amorphous solid (80.4 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, J = 15.5 Hz, 1H), 7.68-7.58 (m, 3H), 7.40 (d, J = 7.6 Hz, 2H), 7.34 (t, J = 7.5 Hz, 2H), 7.17 (d, J = 7.7 Hz, 2H), 7.14-7.07 (m, 1H), 6.54 (d, J = 15.5 Hz, 1H), 2.37 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.3, 142.4, 140.4, 138.1, 131.8, 129.6, 129.1, 128.0, 124.4, 120.0, 119.8, 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{16}H_{16}NO$ $[M+H]^+$: 238.1232; Found: 238.1234.

(*E*)-*N*-(4-(dimethylamino)phenyl)-3-(*p*-tolyl)acrylamide (4b). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and *N,N*-dimethyl-4-nitroaniline (1.0 equiv, 0.50 mmol, 83.1 mg) using petroleum ether/EtOAc (6:1) as an eluent to give the title compound as

a brown amorphous solid (109.9 mg, 78%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.69 (d, J = 15.3 Hz, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 7.5 Hz, 2H), 7.16 (d, J = 7.4 Hz, 2H), 6.72 (d, J = 8.1 Hz, 2H), 6.52 (d, J = 15.4 Hz, 1H), 2.92 (s, 6H), 2.36 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 163.9, 147.8, 141.4, 140.0, 132.1, 129.6, 128.2, 127.9, 121.7, 120.2, 113.2, 41.0, 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{18}H_{21}N_2O$ $[M+H]^+$: 281.1654; Found: 281.1656.

(*E*)-*N*-(4-methoxyphenyl)-3-(*p*-tolyl)acrylamide (4c). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-methoxy-4-nitrobenzene (1.0 equiv, 0.50 mmol, 76.6 mg) using petroleum ether/EtOAc (5:1) as an eluent to give the title compound as a white amorphous solid (88.4 mg, 66%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72 (d, J = 15.5 Hz, 1H), 7.53 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 7.4 Hz, 2H), 7.30 (s, 1H), 7.19 (d, J = 7.5 Hz, 2H), 6.89 (d, J = 8.3 Hz, 2H), 6.49 (d, J = 15.5 Hz, 1H), 3.80 (s, 3H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.0, 156.5, 142.0, 140.3, 131.9, 131.2, 129.6, 127.9, 121.7, 119.8, 114.2, 55.5, 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338; Found: 268.1341.

(*E*)-*N*-(4-(phenylthio)phenyl)-3-(*p*-tolyl)acrylamide (4d). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and (4-nitrophenyl)(phenyl)sulfane (1.0 equiv, 0.50 mmol, 115.6 mg) using petroleum ether/EtOAc (8:1) as an eluent to give the title compound

as a white amorphous solid (149.3 mg, 86%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, J = 15.4 Hz, 1H), 7.59 (d, J = 7.8 Hz, 2H), 7.43 (d, J = 7.5 Hz, 2H), 7.38 (d, J = 7.7 Hz, 2H), 7.34 (s, 1H), 7.28 (m, 4H), 7.19 (d, J = 7.5 Hz, 3H), 6.49 (d, J = 15.4 Hz, 1H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.3, 142.8, 140.6, 137.7, 136.8, 133.0, 131.7, 129.9, 129.7, 129.2, 128.0, 126.6, 120.7, 119.4, 21.5. (15 carbon signals were observed out of expected 16 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{22}H_{20}NOS$ $[M+H]^+$: 346.1266; Found: 346.1270.

(*E*)-*N*,3-di-*p*-tolylacrylamide (4e).[11] Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-methyl-4-nitrobenzene (1.0 equiv, 0.50 mmol, 68.6 mg) using petroleum ether/EtOAc (12:1) as an eluent to give the title compound as a white amorphous solid (68.0 mg, 54%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72 (d, J = 15.4 Hz, 1H), 7.51 (d, J = 7.4 Hz, 2H), 7.41 (d, J = 7.8 Hz, 3H), 7.16 (m, 4H), 6.51 (d, J = 15.5 Hz, 1H), 2.37 (s, 3H), 2.32 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.1, 142.1, 140.3, 135.5, 134.0, 131.9, 129.6, 129.6, 128.0, 120.0, 119.9, 21.5, 20.9.

(*E*)-*N*-(3-methoxy-4-methylphenyl)-3-(*p*-tolyl)acrylamide (4f). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 2-methoxy-1-methyl-4-nitrobenzene (1.0 equiv, 0.50 mmol, 83.6 mg) using petroleum ether/EtOAc (9:1) as an eluent to give the title compound as a white amorphous solid (95.9 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$):

δ 7.72 (d, J = 15.4 Hz, 1H), 7.54 (s, 1H), 7.47 (s, 1H), 7.40 (d, J = 7.6 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 7.05 (d, J = 7.9 Hz, 1H), 6.83 (d, J = 7.8 Hz, 1H), 6.51 (d, J = 15.5 Hz, 1H), 3.83 (s, 3H), 2.37 (s, 3H), 2.18 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.2, 158.0, 142.2, 140.3, 137.1, 131.9, 130.4, 129.6, 127.9, 122.7, 119.9, 111.2, 102.9, 55.35, 21.4, 15.8. **HRMS** (ESI): *m/z* Calc. for $C_{18}H_{20}NO_2$ $[M+H]^+$: 282.1494; Found: 282.1499.

(*E*)-*N*-(2,4-dimethylphenyl)-3-(*p*-tolyl)acrylamide (4g). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 2,4-dimethyl-1-nitrobenzene (1.0 equiv, 0.50 mmol, 75.6 mg) using petroleum ether/EtOAc (10:1) as an eluent to give the title compound as a white amorphous solid (68.6 mg, 52%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79 (s, 1H), 7.73 (d, J = 15.3 Hz, 1H), 7.44 (s, 2H), 7.19 (d, J = 6.2 Hz, 2H), 7.04 (d, J = 8.1 Hz, 3H), 6.54 (d, J = 14.9 Hz, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.27 (s, 3H). **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$): δ 164.2, 142.1, 140.3, 134.9, 133.2, 132.0, 131.2, 129.6, 129.1, 128.0, 127.4, 123.3, 119.7, 21.5, 21.0, 17.9. **HRMS** (ESI): *m/z* Calc. for $C_{18}H_{20}NO$ $[M+H]^+$: 266.1545; Found: 266.1549.

(*E*)-*N*-(4-(*tert*-butyl)phenyl)-3-(*p*-tolyl)acrylamide (4h).[45] Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-(*tert*-butyl)-4-nitrobenzene (1.0 equiv, 0.50 mmol, 899 mg) using petroleum ether/EtOAc (14:1) as an eluent to give the title compound as

a white amorphous solid (90.9 mg, 58%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, J = 15.5 Hz, 1H), 7.53 (s, 2H), 7.44 (s, 1H), 7.41 (d, J = 7.6 Hz, 2H), 7.35 (d, J = 7.9 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 6.52 (d, J = 15.5 Hz, 1H), 2.36 (s, 3H), 1.31 (s, 9H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.4, 147.3, 142.1, 140.2, 135.6, 132.0, 129.6, 128.0, 125.9, 120.0, 119.9, 34.4, 31.4, 21.5.

(*E*)-*N*-(3-chlorophenyl)-3-(*p*-tolyl)acrylamide (4i). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-chloro-3-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (14:1) as an eluent to give the title compound as a pale yellow amorphous solid (97.0 mg, 71%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.79-7.67 (m, 2H), 7.46 (d, J = 8.1 Hz, 1H), 7.42 (d, J = 7.8 Hz, 3H), 7.29-7.22 (m, 1H), 7.18 (d, J = 7.6 Hz, 2H), 7.09 (d, J = 7.9 Hz, 1H), 6.49 (d, J = 15.5 Hz, 1H), 2.37 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.2, 143.1, 140.6, 139.3, 134.7, 131.7, 130.0, 129.7, 128.0, 124.4, 120.1, 119.2, 117.9, 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{16}H_{15}NOCl$ $[M+H]^+$: 272.0842; Found: 272.0839.

(*E*)-*N*-(4-fluorophenyl)-3-(*p*-tolyl)acrylamide (4j). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-fluoro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 70.6 mg) using petroleum ether/EtOAc (9:1) as an eluent to give the title compound as a white amorphous solid (83.2 mg, 65%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.72 (d, J = 15.5 Hz,

1H), 7.57 (s, 2H), 7.42 (d, J = 7.5 Hz, 2H), 7.37 (s, 1H), 7.19 (d, J = 7.6 Hz, 2H), 7.03 (t, J = 8.2 Hz, 2H), 6.49 (d, J = 15.5 Hz, 1H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.3, 159.4 (d, $^{1}J_{CF}$ = 245.97 Hz), 142.6, 140.5, 134.1, 131.8, 129.6, 128.0, 121.8 (d, $^{3}J_{CF}$ = 7.33 Hz), 119.5, 115.7 (d, $^{2}J_{CF}$ = 22.52 Hz), 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{16}H_{15}NOF$ $[M+H]^+$: 256.1138; Found: 256.1139.

(*E*)-*N*-(4-bromophenyl)-3-(*p*-tolyl)acrylamide (4k). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-bromo-4-nitrobenzene (1.0 equiv, 0.50 mmol, 101.0 mg) using petroleum ether/EtOAc (12:1) as an eluent to give the title compound as a white amorphous solid (124.9 mg, 79%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.73 (d, J = 15.4 Hz, 1H), 7.53 (d, J = 7.6 Hz, 2H), 7.48-7.41 (m, 4H), 7.36 (s, 1H), 7.20 (d, J = 7.4 Hz, 2H), 6.49 (d, J = 15.5 Hz, 1H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.1, 142.9, 140.6, 137.2, 132.1, 131.7, 129.7, 128.0, 121.5, 119.3, 117.0, 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{16}H_{15}NOBr$ $[M+H]^+$: 316.0337; Found: 316.0342.

(*E*)-3-(*p*-tolyl)-*N*-(3-(trifluoromethyl)phenyl)acrylamide (4l). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-nitro-3-(trifluoromethyl)benzene (1.0 equiv, 0.50 mmol, 95.6 mg) using petroleum ether/EtOAc (12:1) as an eluent to give the title compound as a white amorphous solid (134.7 mg, 88%). **^{1}H NMR** (400 MHz, DMSO-d_6): δ 10.53 (s, 1H), 8.23 (s, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.67-7.50 (m, 4H), 7.42 (d,

J = 7.7 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 15.7 Hz, 1H), 2.35 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6): δ 164.6, 141.4, 140.6, 140.4, 132.2, 130.5, 130.1, 130.0 (q, $^{2}J_{CF}$ = 31.7 Hz), 128.3, 124.6 (q, $^{1}J_{CF}$ = 272.2 Hz), 123.2, 121.1, 120.1 (q, $^{3}J_{CF}$ = 3.9 Hz), 115.7 (q, $^{3}J_{CF}$ = 4.0 Hz), 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{17}H_{15}NOF_3$ $[M+H]^+$: 306.1106; Found: 306.1110.

(*E*)-3-(*p*-tolyl)-*N*-(4-(trifluoromethyl)phenyl)acrylamide (4m). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-nitro-4-(trifluoromethyl)benzene (1.0 equiv, 0.50 mmol, 95.6 mg) using petroleum ether/EtOAc (13:1) as an eluent to give the title compound as a pain yellow amorphous solid (97.6 mg, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.81-7.69 (m, 3H), 7.60 (d, *J* = 8.1 Hz, 2H), 7.52 (s, 1H), 7.43 (d, *J* = 7.4 Hz, 2H), 7.20 (d, *J* = 7.4 Hz, 2H), 6.51 (d, *J* = 15.4 Hz, 1H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6): δ 164.7, 143.4, 141.5, 140.4, 132.3, 130.1, 128.3, 126.6 (q, $^{3}J_{CF}$ = 3.6 Hz), 124.9 (q, $^{1}J_{CF}$ = 271.3 Hz), 123.7 (q, $^{2}J_{CF}$ = 32.1 Hz). 121.2, 119.6, 21.4. **HRMS**(ESI): *m/z* Calc. for $C_{17}H_{15}NOF_3$ $[M+H]^+$: 306.1106; Found: 306.1115.

(*E*)-*N*-(3-cyano-4-methylphenyl)-3-(*p*-tolyl)acrylamide (4n). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 2-methyl-5-nitrobenzonitrile (1.0 equiv, 0.50 mmol, 81.1 mg) using petroleum ether/EtOAc (5:1) as an eluent to give the title compound as a pale yellow amorphous solid (99.4 mg, 72%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.93

(s, 1H), 7.80-7.68 (m, 2H), 7.44 (d, J = 7.6 Hz, 2H), 7.39 (s, 1H), 7.29 (d, J = 8.7 Hz, 1H), 7.21 (d, J = 7.6 Hz, 2H), 6.49 (d, J = 15.3 Hz, 1H)), 2.52 (s, 3H), 2.39 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 143.4, 140.8, 137.6, 136.4, 131.6, 130.9, 129.7, 128.1, 124.1, 123.2, 118.9, 118.8, 113.2, 21.5, 19.9. (15 carbon signals were observed out of expected 16 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{18}H_{17}N_2O$ $[M+H]^+$: 277.1341; Found: 277.1348.

(*E*)-*N*-(4-(*N*,*N*-diethylsulfamoyl)phenyl)-3-(*p*-tolyl)acrylamide (4o). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and *N*,*N*-diethyl-4-nitrobenzenesulfonamide (1.0 equiv, 0.50 mmol, 129.2 mg) using petroleum ether/EtOAc (4:1) as an eluent to give the title compound as a pale yellow amorphous solid (102.1 mg, 55%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.83 (s, 1H), 7.81-7.72 (m, 5H), 7.44 (d, J = 7.6 Hz, 2H), 7.20 (d, J = 7.6 Hz, 2H), 6.56 (d, J = 15.4 Hz, 1H), 3.23 (q, J = 6.9 Hz, 4H), 2.38 (s, 3H), 1.13 (t, J = 6.9 Hz, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.5, 143.5, 141.9, 140.8, 135.1, 131.6, 129.7, 128.3, 128.1, 119.5, 119.1, 42.1, 21.5, 14.2. **HRMS** (ESI): *m/z* Calc. for $C_{20}H_{25}N_2O_3S$ $[M+H]^+$: 373.1586; Found: 373.1585.

(*E*)-*N*-(benzo[*d*][1,3]dioxol-5-yl)-3-(*p*-tolyl)acrylamide (4p). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 5-nitrobenzo[*d*][1,3]dioxole (1.0 equiv, 0.50 mmol, 83.6 mg) using petroleum ether/EtOAc (6:1) as an eluent to give the title compound as

a white amorphous solid (90.3 mg, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.71 (d, J = 15.5 Hz, 1H), 7.43 (d, J = 7.6 Hz, 2H), 7.38 (s, 1H), 7.30 (s, 1H), 7.19 (d, J = 7.6 Hz, 2H), 6.88 (d, J = 8.3 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 6.47 (d, J = 15.4 Hz, 1H), 5.96 (s, 2H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.0, 147.9, 142.3, 140.4, 131.9, 129.6, 128.0, 119.6, 113.0, 108.1, 102.8, 101.3, 21.5. (13 carbon signals were observed out of expected 15 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{17}H_{16}NO_3$ $[M+H]^+$: 282.1130; Found: 282.1129.

(*E*)-*N*-(benzo[*d*]thiazol-6-yl)-3-(*p*-tolyl)acrylamide (4q). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 6-nitrobenzo[*d*]thiazole (1.0 equiv, 0.50 mmol, 90.1 mg) using petroleum ether/EtOAc (3:1) as an eluent to give the title compound as a brown amorphous solid (93.9 mg, 64%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.93 (s, 1H), 8.73 (s, 1H), 8.05 (d, J = 8.7 Hz, 1H), 7.85 (s, 1H), 7.77 (d, J = 15.4 Hz, 1H), 7.42 (d, J = 7.7 Hz, 2H), 7.18 (d, J = 7.7 Hz, 2H), 6.58 (d, J = 15.5 Hz, 1H), 2.38 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.4, 153.5, 150.0, 142.9, 140.6, 135.9, 135.0, 131.7, 129.7, 128.0, 123.6, 119.4, 119.0, 112.6, 21.5. **HRMS** (ESI): *m/z* Calc. for $C_{17}H_{15}N_2OS$ $[M+H]^+$: 295.0905; Found: 295.0909.

(*E*)-*N*-(1-benzyl-1*H*-indol-5-yl)-3-(*p*-tolyl)acrylamide (4r). Following the general procedure A, the title compound was prepared using (*E*)-3-(*p*-tolyl)acrylic acid (1.2 equiv, 0.60 mmol, 97.3 mg) and 1-benzyl-5-nitro-1*H*-indole (1.0 equiv, 0.50 mmol,

75.6 mg) using petroleum ether/EtOAc (8:1) as an eluent to give the title compound as a pale yellow amorphous solid (85.8 mg, 47%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.73 (d, J = 15.5 Hz, 1H), 7.44 (d, J = 7.4 Hz, 2H), 7.40 (s, 1H), 7.34-7.27 (m, 4H), 7.22 (s, 1H), 7.18 (d, J = 8.1 Hz, 2H), 7.14 (s, 1H), 7.09 (d, J = 6.7 Hz, 2H), 6.59-6.47 (m, 2H), 5.31 (s, 2H), 2.37 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.0, 141.6, 140.0, 137.4, 132.2, 130.6, 129.6, 129.2, 128.9, 128.8, 127.9, 127.7, 126.7, 120.3, 116.0, 112.8, 109.9, 102.0, 50.3, 21.4. (20 carbon signals were observed out of expected 21 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{25}H_{23}N_2O$ $[M+H]^+$: 367.1810; Found: 367.1805.

5-(2,5-dimethylphenoxy)-2,2-dimethyl-*N*-(quinolin-6-yl)pentanamide (4s). Following the general procedure A, the title compound was prepared using Gemfibrozil (1.2 equiv, 0.60 mmol, 150.2 mg) and 6-nitroquinoline (1.0 equiv, 0.50 mmol, 87.1 mg). But after the reaction was complete, the mixture was quenched with water (~10 mL) followed by 1 M HCl solution (~0.5 mL, for the protonation of amide anion to form amide). The reaction mixture was then neutralized with 0.5 M NaOH solution (~10 mL), and the aqueous phase was extracted three times with ethyl acetate (EtOAc, ~3×20 mL). The combined organic fraction was further washed with saturated NaCl solution, dried with anhydrous Na_2SO_4, and then concentrated in *vacuo* with the aid of a rotary evaporator. The residue was purified by flash column chromatography using petroleum ether/EtOAc (2:1) as an eluent to give the title compound as a white amorphous solid (69.5 mg, 37 %). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.82 (s, 1H), 8.42 (s, 1H), 8.07 (dd, J

= 25.0, 8.3 Hz, 2H), 7.74 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.38 (s, 1H), 6.99 (d, *J* = 6.8 Hz, 1H), 6.65 (d, *J* = 6.7 Hz, 1H), 6.59 (s, 1H), 3.95 (s, 2H), 2.26 (s, 3H), 2.17 (s, 3H), 1.87 (s, 4H), 1.39 (s, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 176.3, 156.8, 149.1, 145.1, 136.6, 136.3, 135.9, 130.4, 129.7, 128.9, 123.7, 123.5, 121.7, 120.9, 116.4, 112.2, 67.8, 43.1, 37.7, 25.7, 25.2, 21.4, 15.9. **HRMS** (ESI): *m/z* Calc. for $C_{24}H_{29}N_2O_2$ $[M+H]^+$: 377.2224; Found: 377.2217.

2-(4-chloro-2-methylphenoxy)-*N*-(4-chlorophenyl)acetamide (5a). Following the general procedure A, the title compound was prepared using MCPA (1.2 equiv, 0.60 mmol, 120.4 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (15:1) as an eluent to give the title compound as a white amorphous solid (94.7 mg, 61%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.3 Hz, 2H), 7.20 (s, 1H), 7.16 (d, *J* = 8.8 Hz, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 4.58 (s, 2H), 2.34 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 166.0, 153.8, 135.3, 131.1, 130.0, 129.2, 128.4, 127.2, 127.1, 121.2, 113.1, 68.0, 16.3. **HRMS (ESI):** *m/z* Calc. for $C_{15}H_{13}Cl_2NNaO_2$ $[M+Na]^+$: 332.0216; Found: 332.0216.

***N*-(4-chlorophenyl)-2-(6-methoxynaphthalen-2-yl)propenamide (5b)**. Following the general procedure A, the title compound was prepared using Naproxen (1.2 equiv, 0.60 mmol, 138.2 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (10:1) as an eluent to give the title compound as a white amorphous solid (117.5 mg, 70%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.80-7.68 (m, 3H),

7.41 (d, J = 8.4 Hz, 1H), 7.35 (d, J = 8.3 Hz, 2H), 7.24-7.16 (m, 3H), 7.16-7.09 (m, 2H), 3.93 (s, 3H), 3.83 (q, J = 6.9 Hz, 1H), 1.66 (d, J = 7.0 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 172.5, 156.0, 136.4, 135.7, 134.0, 129.3, 129.2, 129.0, 128.9, 128.0, 126.4, 126.1, 120.9, 119.5, 105.7, 55.4, 48.1, 18.5. **HRMS** (ESI): *m/z* Calc. for $C_{20}H_{18}ClNNaO_2$ $[M+Na]^+$: 362.0918; Found: 362.0913.

***N*-(4-chlorophenyl)-2-(4-isobutylphenyl)propenamide (5c).** Following the general procedure A, the title compound was prepared using Ibuprofen (1.2 equiv, 0.60 mmol, 123.8 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (17:1) as an eluent to give the title compound as a white amorphous solid (137.7 mg, 87%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.36 (d, J = 8.4 Hz, 2H), 7.29-7.19 (m, 4H), 7.16 (d, J = 7.5 Hz, 2H), 7.04 (s, 1H), 3.68 (q, J = 6.9 Hz, 1H), 2.47 (d, J = 7.0 Hz, 2H), 1.93-1.80 (m, 1H), 1.58 (d, J = 7.0 Hz, 3H), 0.91 (d, J = 6.5 Hz, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 172.6, 141.3, 137.8, 136.5, 130.0, 129.1, 128.9, 127.4, 120.9, 47.8, 45.0, 30.2, 22.4, 18.5. **HRMS** (ESI): *m/z* Calc. for $C_{19}H_{22}ClNNaO^+$ $[M+Na]^+$: 338.1282; Found: 338.1287.

***N*-(4-chlorophenyl)-4-(*N*,*N*-dipropylsulfamoyl)benzamide (5d).** Following the general procedure A, the title compound was prepared using Probenecid (1.2 equiv, 0.60 mmol, 171.2 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (8:1) as an eluent to give the title compound as a pale yellow amorphous solid (134.8 mg, 68%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.38 (s, 1H),

7.91 (d, J = 7.9 Hz, 2H), 7.74 (d, J = 7.9 Hz, 2H), 7.67 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 3.07 (t, J = 7.3 Hz, 4H), 1.53 (dd, J = 14.4, 7.2 Hz, 4H), 0.86 (t, J = 7.1 Hz, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 164.7, 142.8, 138.6, 136.4, 129.9, 129.13, 128.0, 127.3, 121.5, 50.0, 21.9, 11.2. **HRMS** (ESI): *m/z* Calc. for $C_{19}H_{24}ClN_2O_3S$ $[M+H]^+$: 395.1191; Found: 395.1192.

***N*-(4-chlorophenyl)-5-(2,5-dimethylphenoxy)-2,2-dimethylpentanamide (5e).** Following the general procedure A, the title compound was prepared using Gemfibrozil (1.2 equiv, 0.60 mmol, 150.2 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (24:1) as an eluent to give the title compound as a white amorphous solid (135.9 mg, 76%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.46 (d, J = 8.1 Hz, 2H), 7.35 (s, 1H), 7.27 (d, J = 8.4 Hz, 2H), 7.00 (d, J = 7.4 Hz, 1H), 6.66 (d, J = 7.5 Hz, 1H), 6.60 (s, 1H), 3.94 (s, 2H), 2.29 (s, 3H), 2.16 (s, 3H), 1.81 (s, 4H), 1.33 (s, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 175.7, 156.8, 136.6, 136.5, 130.4, 129.3, 129.0, 123.5, 121.4, 120.9, 112.2, 67.8, 42.9, 37.6, 25.6, 25.1, 21.4, 15.9. **HRMS** (ESI): *m/z* Calc. for $C_{21}H_{26}ClNNaO_2$ $[M+Na]^+$: 382.1544; Found: 382.1541.

(4*R*)-*N*-(4-chlorophenyl)-4-((8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-3,7,12-trioxohexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanamide (5f). Following the general procedure A, the title compound was prepared using dehydrocholic acid (1.2 equiv, 0.60 mmol, 241.5 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (2:1) as an eluent to give the

title compound as a pale yellow amorphous solid (64.3 mg, 41%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.48 (m, 3H), 7.26 (m, 2H), 3.00-2.77 (m, 3H), 2.52-2.11 (m, 10H), 2.09-1.81 (m, 6H), 1.62 (m, 1H), 1.46-1.25 (m, 7H), 1.07 (s, 3H), 0.86 (d, J = 6.4 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 212.2, 209.2, 209.0, 171.7, 136.6, 129.0, 121.0, 56.9, 51.8, 49.0, 46.8, 45.5, 45.4, 45.0, 42.8, 38.7, 36.5, 36.0, 35.4, 35.3, 34.3, 30.7, 27.7, 25.2, 21.9, 18.8, 11.9. (27 carbon signals were observed out of expected 28 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{30}H_{38}ClNNaO_4$ $[M+Na]^+$: 534.2382; Found: 534.2387.

4-chloro-*N*-(4-((1-((4-chlorophenyl)amino)-2-methyl-1-oxopropan-2-yl)oxy)phenethyl)benzamide (5g). Following the general procedure A, the title compound was prepared using Bezafibrate (1.2 equiv, 0.60 mmol, 217.1 mg) and 1-chloro-4-nitrobenzene (1.0 equiv, 0.50 mmol, 78.8 mg) using petroleum ether/EtOAc (4:1) as an eluent to give the title compound as a white amorphous solid (96.6 mg, 41%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.60 (s, 1H), 7.63 (d, J = 7.9 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 7.9 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 6.94 (d, J = 7.8 Hz, 2H), 6.10 (s, 1H), 3.69 (dd, J = 12.8, 6.4 Hz, 2H), 2.91 (t, J = 6.8 Hz, 2H), 1.57 (s, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 173.0, 166.4, 152.5, 137.8, 136.1, 134.4, 132.9, 129.8, 129.5, 129.1, 128.9, 128.2, 122.2, 121.0, 82.0, 41.3, 35.0, 24.9. **HRMS** (ESI): *m/z* Calc. for $C_{25}H_{24}Cl_2N_2NaO_3$ $[M+Na]^+$: 493.1056; Found: 493.1049.

***N*-(3-isopropoxyphenyl)-2-methylbenzamide (Mepronil, 5h).** Following the general procedure A, the title compound was prepared using 2-methylbenzoic acid (1.2 equiv, 0.60 mmol, 81.6 mg) and 1-isopropoxy-3-nitrobenzene (1.0 equiv, 0.50 mmol, 90.6 mg) using petroleum ether/EtOAc (17:1) as an eluent to give the title compound as a pale yellow amorphous solid (111.4 mg, 83%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 7.52-7.41 (m, 2H), 7.41-7.32 (m, 2H), 7.25 (m, 3H), 7.05 (d, J = 7.2 Hz, 1H), 6.69 (d, J = 8.1 Hz, 1H), 4.68-4.52 (m, 1H), 2.50 (s, 3H), 1.35 (d, J = 5.7 Hz, 6H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 168.0, 158.6, 139.2, 136.5, 136.4, 131.3, 130.3, 129.8, 126.6, 125.9, 112.2, 111.8, 107.5, 70.0, 22.1, 19.8. **HRMS** (ESI): *m/z* Calc. for $C_{17}H_{19}NNaO_2^+$ $[M+Na]^+$: 292.1308; Found: 292.1302.

***N*-(2-phenylbenzo[*d*]oxazol-5-yl)benzamide (5i).** Following the general procedure A, the title compound was prepared using benzoic acid (1.2 equiv, 0.60 mmol, 61.1 mg) and 5-nitro-2-phenylbenzo[*d*]oxazole (1.0 equiv, 0.50 mmol, 120.1 mg) using petroleum ether/EtOAc (7:1) as an eluent to give the title compound as a pale yellow amorphous solid (55.9 mg, 36%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 8.25 (d, J = 6.1 Hz, 2H), 8.03 (s, 2H), 7.90 (d, J = 7.2 Hz, 2H), 7.66 (d, J = 8.6 Hz, 1H), 7.60-7.43 (m, 7H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ 166.0, 164.2, 148.0, 142.8, 135.0, 132.1, 131.8, 129.1, 129.0, 127.8, 127.2, 127.1, 118.8, 112.2, 110.8. (15 carbon signals were observed out of expected 16 carbon signals). **HRMS** (ESI): *m/z* Calc. for $C_{20}H_{14}N_2NaO_2$ $[M+Na]^+$: 337.0947; Found: 337.0948.

3,5-dichloro-*N*-(2-methylbenzo[*d*]thiazol-5-yl)benzamide (5j). Following the general procedure A, the title compound was prepared using 3,5-dichlorobenzoic acid (1.2 equiv, 0.60 mmol, 114.6 mg) and 2-methyl-5-nitrobenzo[*d*]thiazole (1.0 equiv, 0.50 mmol, 97.1 mg) using petroleum ether/EtOAc (14:1) as an eluent to give the title compound as a white amorphous solid (88.3 mg, 53%). **^{1}H NMR** (400 MHz, DMSO-d_6): δ 10.61 (s, 1H), 8.37 (s, 1H), 8.01 (s, 2H), 7.98 (d, J = 8.8 Hz, 1H), 7.89 (s, 1H), 7.69 (d, J = 8.6 Hz, 1H), 2.80 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6): δ 169.6, 163.3, 153.8, 138.5, 137.9, 134.8, 131.5, 130.2, 127.0, 122.0, 118.0, 112.9, 16.0. **HRMS** (ESI): *m/z* Calc. for $C_{15}H_{11}N_2OSCl_2$ $[M+H]^+$: 336.9969; Found: 336.9961

SUPPORTING INFORMATION

Copies of ^{1}H and ^{13}C NMR spectra for all products (pdf). The material is available free of charge via the internet http://pubs.acs.org.

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