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Condensation of Carboxylic Acids with Non-Nucleophilic N-Heterocycles and Anilides Using Boc₂O

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ABSTRACT: A novel condensation reaction of carboxylic acids with various non-nucleophilic *N*-heterocycles and anilides was developed. The reaction proceeds in the presence of di-*tert*-butyl dicarbonate (Boc₂O), catalytic 4-(dimethylamino)pyridine (DMAP), and 2,6-lutidine and is applicable to the acylation of a wide range of non-nucleophilic nitrogen compounds, including indoles, pyrroles, pyrazole, carbazole, lactams, oxazolidinones, and anilides with high functional group compatibility. The scope of indoles, carboxylic acids, and anilides was also studied.

The amide group is one of the most important and fundamental functional groups present in naturally occurring compounds, proteins, synthetic polymers, and pharmaceutical agents. Therefore, the development of amide formation reactions has a long history, and numerous reaction conditions have so far been reported.¹ However, methodologies for the direct condensation of carboxylic acids with aromatic *N*-heterocycles such as indole, pyrrole, pyrazole, and carbazole are limited² due the low nucleophilicity of these substrates, which is attributed to the participation of the nitrogen lone pair electrons in the aromatic system. Direct condensation of lactams or anilides is also inefficient, due to the low nucleophilicity of the nitrogen lone pair electrons into the carbonyl group.

In order to conduct condensation reactions of these nonnucleophilic nitrogen compounds with carboxylic acids, prior formation of an anionic species by deprotonation of the N–H by a stoichiometric strong metal base such as *n*-butyllithium or NaH and/or the use of an activated carboxylic acid derivative such as an acid halide or activated ester^{3,4,5} is usually required. For example, Snider reported *N*-acylation of a tryptophan derivative by using a *p*-nitrophenyl ester as an acylation reagent.⁶ Sarpong has recently demonstrated that carbonylazoles are effective for a highly chemoselective *N*acylation of indoles and oxazolidinones.⁷

To consider a direct condensation of carboxylic acids and non-nucleophilic nitrogen compounds, we focused on the function of di-*tert*-butyl dicarbonate (Boc₂O). Installation of a *tert*-butyloxycarbonyl (Boc) group on a variety of nonnucleophilic nitrogen compounds including indoles, pyrroles, and lactams proceeds smoothly with a combination of Boc₂O and 4-(dimethylamino)pyridine (DMAP).⁸ This process should include *in situ* generation of a *N*-Bocdimethylaminopyridinium ion and naked *t*-butoxide.^{8d} On the other hand, a combination of Boc₂O, DMAP, and tertiary amines or pyridine is effective for condensation of carboxylic acids with primary amines,^{9a} anilines,^{9b} ammonia,^{9c} alcohols,^{9d-g} or phenols,^{9d} in which the corresponding mixed anhydride is initially formed.

We reasoned that upon mixing a non-nucleophilic nitrogen compound, such as indole (1), and a carboxylic acid in the presence of Boc₂O and DMAP, the above Boc-mediated processes would facilitate acylation to form N-acylated product 6 by activation of the carboxylic acid as a mixed anhydride 2 or N-acyl-dimethylaminopyridinium ion 3 and activation of the non-nucleophilic nitrogen compound as an anionic species (Scheme 1).¹⁰ A competing process would be the formation of *N*-Boc-indole^{8b, 8c, 8e, 8f} 7 and/or a *t*-butyl ester9e, 9g 8 via reaction of the indole anion with N-Bocdimethylaminopyridinium ion 5 or reaction of *t*-butoxide with mixed anhydride 2 or N-acyl-dimethylaminopyridinium ion 3, respectively. To the best of our knowledge, Boc-mediated condensation has only been applied to intrinsically nucleophilic compounds⁹ and there is no report on nonnucleophilic nitrogen compounds. Herein, we report a novel direct condensation of carboxylic acids with various nonlactams, nucleophilic aromatic N-heterocycles, oxazolidinones, and anilides under metal-free mild conditions using Boc₂O.

Scheme 1. Working Hypothesis.



Keeping these considerations in mind, we examined the proposed Boc₂O-mediated amide formation using monomethyl succinate (9a) and indole (1) as test substrates (Table 1). First, we tested the conditions required for Boc protection of the indole N-H (entry 1). Thus, 1 was treated with 9a in the presence of Boc₂O and 5 mol% DMAP. To our satisfaction, we obtained a moderate yield of the expected N-acylindole **10a** along with a trace amount of *N*-Boc-indole 7, without the *t*-butyl ester of **9a** being formed. Reactions with other amine catalysts such as *N*-methylimidazole (NMI), 1.4diazabicyclo[2.2.2]octane (DABCO), and 1.8diazabicyclo[5.4.0]undec-7-ene (DBU) (entries 2-4) did not give amide 10a in better yields. Considering that protonation of DMAP with the carboxylic acid would prevent smooth conversion, we then added additional base to the reaction. A significant acceleration was observed when we added 10 mol% triethylamine to give 10a in 87% yield (entry 5). Extensive examination revealed that 2,6-lutidine vielded the best result, thus affording the desired *N*-acylindole **10a** in 92% vield (entry 7). In addition, the reaction using inorganic bases proceeded smoothly to provide the desired product 10a in high yields (entries 8–11). The reaction did not proceed without DMAP at all (entry 12), thus indicating that it plays a crucial role in this condensation reaction. The yield decreased when CH_2Cl_2 was used as the solvent instead of MeCN (entry 13). Excess indole and Boc₂O are also necessary for the high-yielding and selective formation of *N*-acylindole **10a**. Thus, a reaction using an equimolar amount of **1** with Boc₂O (1.5 equiv.) gave **10a** in 65% yield along with *N*-Boc-indole **7** (14%) and recovery of **1** (21%) (entry 14). Moreover, we performed this reaction using 5 gram of carboxylic acid **9a**. The reaction proceeded uneventfully to afford the target acyl indole **10a** in almost quantitative yield (entry 15).

Table 1. Optimization of Reaction Conditions.

		1 Boc ₂ C (2.5 eq) additive	D (2.5 eq) t (5 mol%) e (10 mol%)	N.		
	0H + 0 9a	⊢ N CO₂Me 28° a	leCN C, 24 h	OCO ₂ Me		
	entry	catalyst	additive	yield (%) ^a		
	1	DMAP	_	42		
	2	NMI	_	33		
	3	DABCO	_	Trace		
	4	DBU	_	0		
	5	DMAP	Et₃N	87		
	6	DMAP	pyridine	88		
	7	DMAP	2,6-lutidine	92		
	8	DMAP	NaHCO ₃	81		
	9	DMAP	Na ₂ CO ₃	79		
	10	DMAP	K ₂ CO ₃	89		
	11	DMAP	Cs_2CO_3	91		
	12	_	2,6-lutidine	0		
	13 ^b	DMAP	2,6-lutidine	69		
	14 ^c	DMAP	2,6-lutidine	65 (82) ^d		
	15 ^e	DMAP	2,6-lutidine	97		
т	1 / 1 .	11 bott of	1. / 1.014	CD 1 (T 1 1 (1		

^{*a*}Isolated yield. ^{*b*}CH₂Cl₂ was used instead of MeCN. ^{*c*}Indole (1 equiv.) and Boc₂O (1.5 equiv.) were used. ^{*d*}Based on the recovered starting indole. ^{*c*}This reaction was performed on 5 gram scale of **9a**.

Having established the optimal conditions, we then investigated the substrate scope of carboxylic acids (Table 2). Reactions using a series of functionalized linear carboxylic acids (**9b-q**) demonstrated that a variety of functional groups, including ketone, ester, silyl ether, alkenyl, alkynyl, bromoalkyl, substituted phenyl, and thienyl groups, were compatible with the reaction conditions to give the corresponding *N*-acylindoles **10b-q** in good to excellent yields. Sterically hindered β - (**9r**) or α -branched (**9s** and **9t**) carboxylic acids were feasible in the reaction to give **10r**, **10s**, and **10t** in good yields. In particular, *N*-benzyloxycarbonylproline derivative **10t** was obtained without loss of optical purity. Due to the relatively lower reactivity, reaction of aromatic carboxylic acids **9u–w** required increased amounts of the bases (20 mol% DMAP and 30 mol% 2,6-lutidine). Notably, heteroaromatic carboxylic acids, 2-pyridinecarboxylic acid (**9v**), and 2-quinolinecarboxylic acid (**9w**), reacted smoothly to provide *N*-acylindoles **10v** and **10w** in good to excellent yields.

Next, the scope of non-nucleophilic nitrogen compounds was studied using 4-phenylbutyric acid (9j) (Table 3). Reaction of 6-, 5-, or 3-substituted indoles bearing halogen or electron-withdrawing groups proceeded well under the optimal conditions to provide *N*-acylindoles (12a-e) in excellent yields. Significantly, 2- and 7-substituted indoles, which usually behave as poor nucleophiles due to steric hindrance, ^{3f,7} gave the corresponding *N*-acylindoles (12f-j) in excellent yields, except for 2-phenylindole (11h). In addition to these indole derivatives, analogous non-nucleophilic *N*-heteroaromatic compounds such as pyrroles, pyrazole, and carbazole proved to be suitable substrates to give *N*-acyl products 12k-n in good to excellent yields.

Table 2. Scope of Carboxylic Acids.^a









^{*a*}Isolated yield.

Furthermore, we found that this reaction was applicable to other non-nucleophilic nitrogen compounds including ylactams, oxazolidinones, and anilides. Thus, γ -lactams (13a and 13b) and oxazolidinones (13c-e) reacted smoothly to provide the corresponding N-acyl products 14a, 14b, and 14ce (Table 4). The anilides (13f-p) bearing substituents at the ortho-, meta- or para-positions on the benzene ring gave the corresponding imides (14f-p) in nearly quantitative yields. Importantly, the sterically hindered substrate 13n derived from 2,6-dimethylaniline reacted uneventfully to furnish the desired imide 14n in a high yield. Finally, 1-aminonaphthalene derivative 130 and 2-pyridylamide 13p served as good substrates to give the desired products (140 and 14p) in excellent and satisfactory yields, respectively. In the case of oxazolidinones (13d and 13e) and anilides (13k, 13l, and 13o), reaction using an equimolar amount of the nucleophiles with Boc_2O (1.5 equiv.) gave the products in high (80–91%) yields.

Plausible reaction mechanisms based on the above observations and related reports⁹ are depicted in Scheme 2. The initial nucleophilic attack of DMAP on Boc₂O should give *N*-Boc-dimethylaminopyridinium ion 5 with concomitant generation of a naked *t*-butoxide anion (4), which deprotonates carboxylic acid 15 to give carboxylate 16, followed by addition of 16 to 5, which would afford mixed anhydride 2. Subsequent nucleophilic attack of DMAP on 2 should produce *N*-acyl-dimethylaminopyridinium ion 3 with formation of naked *t*-butoxide (4). At this point, non-nucleophilic nitrogen compound 17 should be deprotonated by 4 to afford a highly nucleophilic anion 18. Finally, anion 18 would attack 3 to

furnish the desired amide. Smooth acylation of nonnucleophilic nitrogen compounds 17 should be based on dual activation, namely, activation of carboxylic acid by conversion to the *N*-acyl-dimethylaminopyridinium ion **3** and deprotonation of N–H by naked *t*-butoxide (**4**). The key to the selective formation of amides, while circumventing possible competing processes (i.e., formation of *N*-Boc nitrogen compounds and *t*-butyl esters), is attributed to the higher reactivity of **3** among the three acyl donors **2**, **3**, and **5** due to steric as well as electronic reasons. According to the series of experiments in Table 1, we consider that the role of the additional base (2,6-lutidine) would be as a proton scavenger to prevent protonation of DMAP (Scheme 2b).

Table 4. Scope of Lactams, Oxazolidinones, and Anilides.^a



^{*a*}Isolated yield. ^{*b*}Nucleophile (1 equiv.) and Boc₂O (1.5 equiv.) were used.

To demonstrate the practical synthetic utility of the direct condensation, we performed a multi-gram scale reaction (Scheme 3). Thus, acid **9j** and an equimolar amount of anilide **13o** with Boc₂O (1.5 equiv.) were subjected to the reaction conditions. As expected, the condensation took place smoothly to furnish the desired product **14o** in 94% yield.





In conclusion, we have developed a direct condensation of carboxylic acids with a wide variety of non-nucleophilic Nheterocycles such as indoles, pyrroles, pyrazole, carbazole, lactams, and oxazolidinones using the Boc₂O/DMAP/2,6lutidine system. Furthermore, various anilides were also amenable to this reaction and generated imides. The Boc₂O/DMAP/2,6-lutidine system played a crucial role in the in situ dual activation of both carboxylic acids as the N-acyldimethylaminopyridinium ion and of non-nucleophilic nitrogen compounds through the generation of the corresponding anion with naked t-butoxide. This condensation reaction is performed using a simple operation that does not involve prior formation of the anion by deprotonation of the nitrogen nucleophile using a metal base and preparation of an activated carboxylic acid such as an acid halide or activated ester

Experimental Section

General Remarks

Materials were obtained from commercial suppliers and used without further purification unless otherwise mentioned. All reactions were carried out in oven-dried glassware under a slight positive pressure of argon unless otherwise noted. Column chromatography was performed on spherical neutral silica gel (63–210 μ m), and flash column chromatography was performed on spherical neutral silica gel (40–50 μ m) using the indicated eluent. Analytical TLC was performed on glass plates precoated with a 0.25 mm thickness of silica gel. All melting points were determined on a micro melting point apparatus and are uncorrected. ¹H-NMR and ¹³C-NMR spectra were recorded at 400 and 600 MHz for ¹H-NMR and (100 and 150 MHz for ¹³C-NMR. For ¹H-NMR spectra, chemical shifts are given from tetramethylsilane (0 ppm) or chloroform (7.24 ppm) as an internal standard. For ¹³C-NMR spectra, chemical shifts are given from chloroform (77.0 ppm) as an internal standard. Mass spectra were realized by ESI method using a time-of-flight mass spectrometer.

General Synthetic Procedure of Condensation Reaction.

Methyl 4-(1H-indol-1-yl)-4-oxobutanoate (10a)

A 10 mL threaded Pvrex test tube equipped with a magnetic stirring bar, a rubber septum, and argon inlet needle was charged with Boc₂O (223 mg, 1.02 mmol). A solution of mono-methyl succinate (9a) (54.0 mg, 0.409 mmol), indole (1) (120 mg, 1.02 mmol), DMAP (2.5 mg, 0.02 mmol), and 2,6lutidine (4.7 µL, 0.04 mmol) in MeCN (0.9 mL) were added to the test tube at room temperature. Then, the reaction mixture was warmed to 28 °C by water bath. After stirring at 28 °C for 24 h, the resulting mixture was concentrated under reduced pressure to give a crude oil, which was purified by silica gel column chromatography (hexanes/AcOEt = 5:1) to give Nacylindole 10a (87.1 mg, 0.377 mmol, 92%); a white solid; Mp 82-83 °C (hexanes-AcOEt): IR (neat) 2953, 1738, 1708. 1454, 1310, 1207, 910, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.43 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.50 (d, J = 3.6 Hz, 1H), 7.34 (dd, J = 7.8, 6.6 Hz, 1H), 7.28 (dd, J = 8.4, 6.6 Hz, 1H), 6.66 (d, J = 3.6 Hz, 1H), 3.74 (s, 3H), 3.27 (t, J =6.6 Hz, 2H), 2.86 (t, J = 6.6 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) & 172.8, 169.8, 135.6, 130.3, 125.2, 124.3, 123.7, 120.9, 116.5, 109.5, 52.0, 30.7, 28.3; HRMS Calcd. for C₁₃H₁₃NNaO₃ [M+Na⁺] 254.0793, found 254.0790.

1-(1H-Indol-1-yl)-4-phenylbutane-1,4-dione (10b)

According to the general procedure described for **10a**, *N*-acylindole **10b** (79.4 mg, 0.287 mmol, 68%) was obtained from 3-benzolypropionic acid (**9b**) (75.0 mg, 0.421 mmol) and indole (**1**) (123 mg, 1.05 mmol); a white solid; Mp 146-148 °C (hexanes-AcOEt); IR (neat) 2949, 1703, 1678, 1453, 1399, 1360, 1311, 1227, 1212, 773, 764, 751 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.43 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 7.2 Hz, 2H), 7.60 (d, *J* = 4.2 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.27 (dd, *J* = 8.4, 6.6 Hz, 1H), 6.68 (d, *J* = 4.2 Hz, 1H), 3.54 (t, *J* = 6.6 Hz, 2H), 3.41 (t, *J* = 6.6 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) 198.0, 170.4, 136.5, 135.7, 133.4, 130.4, 128.7, 128.1, 125.1, 124.6, 123.7, 120.8, 116.6, 109.4, 32.8, 29.8; HRMS Calcd. for C₁₈H₁₅NNaO₂ [M+Na⁺] 300.1000, found 300.0993.

1-(1*H*-Indol-1-yl)-5-phenylpentane-1,5-dione (10c)

According to the general procedure described for **10a**, *N*-acylindole **10c** (71.4 mg, 0.245 mmol, 73%) was obtained from 4-benzoylbutyric acid (**9c**) (64.0 mg, 0.335 mmol) and indole (**1**) (98.0 mg, 0.836 mmol); a white solid; Mp 98-100

°C (hexanes-AcOEt); IR (neat) 2949, 1704, 1685, 1451, 1388, 1338, 1308, 1224, 1209, 768, 750, 690 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.47 (d, J = 7.8 Hz, 1H), 7.99 (d, J = 7.8 Hz, 2H), 7.58–7.55 (m, 3H), 7.47 (dd, J = 8.4, 7.8 Hz, 2H), 7.58–7.55 (m, 3H), 7.27 (dd, J = 7.8, 7.8 Hz, 1H), 6.64 (d, J = 3.6 Hz, 1H), 3.21 (t, J = 7.2 Hz, 2H), 3.07 (t, J = 7.2 Hz, 2H), 2.30 (tt, J = 7.2, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) 199.5, 171.1, 136.7, 135.6, 133.2, 130.4, 128.6, 128.0, 125.1, 124.7, 123.6, 120.8, 116.6, 109.2, 37.2, 34.9, 19.0; HRMS Calcd. for C₁₉H₁₇NNaO₂ [M+Na⁺] 314.1157, found 314.1152.

Methyl 5-(1*H*-indol-1-yl)-5-oxopentanoate (10d)

According to the general procedure described for **10a**, *N*-acylindole **10d** (79.5 mg, 0.324 mmol, 92%) was obtained from glutaric acid *mono*-methyl ester (**9d**) (52.0 mg, 0.355 mmol) and indole (**1**) (104 mg, 0.887 mmol); a white solid; Mp 49-51 °C (hexanes-AcOEt); IR (neat) 2953, 1735, 1706, 1453, 1310, 1207, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.49 (d, *J* = 3.6 Hz, 1H), 7.35 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.27 (dd, *J* = 8.4, 7.8 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 3.70 (s, 3H), 3.01 (t, *J* = 6.6 Hz, 2H), 2.53 (t, *J* = 6.6 Hz, 2H), 2.17 (tt, *J* = 6.6, 6.6 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 173.5, 170.7, 135.6, 130.3, 125.1, 124.5, 123.7, 120.8, 116.6, 109.2, 51.7, 34.7, 32.8, 19.7; HRMS Calcd. for C₁₄H₁₅NNaO₃ [M+Na⁺] 268.0950, found 268.0934.

4-((*tert*-Butyldimethylsilyl)oxy)-1-(1*H*-indol-1-yl)butan-1one (10e)

According to the general procedure described for **10a**, *N*-acylindole **10e** (69.2 mg, 0.218 mmol, 57%) was obtained from carboxylic acid **9e**¹¹ (84.0 mg, 0.385 mmol) and indole (1) (113 mg, 0.964 mmol); a colorless oil; IR (neat) 2949, 1709, 1453, 1206, 1100, 837, 775, 749 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.47 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 4.2 Hz, 1H), 7.35 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.27 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.64 (d, *J* = 4.2 Hz, 1H), 3.76 (t, *J* = 6.0 Hz, 2H), 3.03 (t, *J* = 7.2 Hz, 2H), 2.06 (tt, *J* = 7.2, 6.0 Hz, 2H), 0.90 (s, 9H), 0.06 (s, 6H); ¹³C NMR (150 MHz, CDCl₃) δ 171.6, 135.6, 130.4, 125.0, 124.8, 123.5, 120.8, 116.6, 109.0, 61.7, 32.2, 27.8, 25.9, 18.3, -5.4; HRMS Calcd. for C₁₈H₂₈NO₂Si [M⁺+H] 318.1889, found 318.1873.

1-(1*H*-Indol-1-yl)pent-4-en-1-one (10f)

According to the general procedure described for 10a, N-acylindole 10f (93.4 mg, 0.469 mmol, 87%) was obtained from 4-pentenoic acid (9f) (54.0 mg, 0.537 mmol) and indole (1) (157 mg, 1.34 mmol); a colorless oil; IR (neat) 2953, 1708, 1453, 1387, 1363, 1320, 1307, 1206, 930, 767, 751 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.47 (d, J = 7.8 Hz, 1H), 7.56 (d, J = 8.4 Hz, 1H), 7.46 (d, J = 3.6 Hz, 1H), 7.35 (dd, J = 8.4, 7.2 Hz, 1H), 7.27 (dd, J = 7.8, 7.2 Hz, 1H), 6.64 (d, J = 3.6 Hz, 1H), 5.94 (dddd, J = 17.1, 10.2, 6.0, 6.0 Hz, 1H), 5.14 (d, J =17.1 Hz, 1H), 5.07 (d, J = 10.2 Hz, 1H), 3.02 (t, J = 6.6 Hz, 2H), 2.62–2.58 (m, 2H); ¹³C NMR (150 MHz, CDCl₃)δ 170.7, 136.5, 135.6, 130.3, 125.1, 124.5, 123.6, 120.8, 116.6, 116.0, 109.1, 35.1, 28.4; HRMS Calcd. for C₁₃H₁₄NO [M⁺+H] 200.1075, found 200.1070. Spectroscopic date matched those previously reported.¹²

1-(1*H*-Indol-1-yl)hex-5-yn-1-one (10g)

According to the general procedure described for **10a**, *N*-acylindole **10g** (67.3 mg, 0.319 mmol, 91%) was obtained from 5-hexynoic acid acid (**9g**) (39.0 mg, 0.350 mmol) and indole (**1**) (103 mg, 0.875 mmol); a white solid; Mp 69-70 °C (hexanes-AcOEt); IR (neat) 2954, 1705, 1452, 1389, 1308, 1205, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.50 (d, *J* = 3.6 Hz, 1H), 7.35 (dd, *J* = 8.4, 7.8 Hz, 1H), 7.27 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.65 (d, *J* = 3.6 Hz, 1H), 3.08 (t, *J* = 7.2 Hz, 2H), 2.41 (dt, *J* = 7.2, 2.4 Hz, 2H), 2.07 (tt, *J* = 7.2, 7.2 Hz, 2H), 2.02 (t, *J* = 2.4 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 170.8, 135.6, 130.3, 125.1, 124.5, 123.6, 120.8, 116.6, 109.2, 83.2, 69.5, 34.2, 23.1, 17.8; HRMS Calcd. for C₁₄H₁₄NO [M⁺+H] 212.1075, found 212.1076.

11-Bromo-1-(1*H*-indol-1-yl)undecan-1-one (10h)

According to the general procedure described for **10a**, *N*-acylindole **10h** (76.3 mg, 0.210 mmol, 71%) was obtained from 11-bromoundecanoic acid (**9h**) (79.0 mg, 0.297 mmol) and indole (**1**) (87.0 mg, 0.742 mmol); a white solid; Mp 52-54 °C (hexanes-AcOEt); IR (neat) 2925, 2853, 1709, 1452, 1386, 1338, 1308, 1205, 767, 750 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.47 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.35 (dd, *J* = 8.4, 6.6 Hz, 1H), 7.27 (dd, *J* = 7.8, 6.6 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 3.40 (t, *J* = 7.2 Hz, 2H), 2.91 (t, *J* = 7.2 Hz, 2H), 1.87–1.81 (m, 4H), 1.47–1.30 (m, 12H); ¹³C NMR (150 MHz, CDCl₃) δ 171.6, 135.6, 130.3, 125.1, 124.6, 123.5, 120.8, 116.6, 109.0, 35.9, 34.0, 32.8, 29.33, 29.31, 29.2, 28.7, 28.1, 24.6 (One signal is missing due to overlap); HRMS Calcd. for C₁₉H₂₇BrNO [M⁺+H] 364.1276, found 364.1272.

(Z)-4-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)-1-(1*H*-indol-1-yl)hex-4-en-1-one (10i)

According to the general procedure described for **10a**, *N*-acylindole **10i** (105 mg, 0.281 mmol, 87%) was obtained from carboxylic acid **9i** (88.0 mg, 0.324 mmol) and indole **(1)** (95.0 mg, 0.810 mmol); a colorless oil; IR (neat) 2953, 1710, 1452, 1205, 835, 749 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.47 (d, *J* = 3.6 Hz, 1H), 7.35 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.27 (dd, *J* = 7.8, 7.2 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 5.39 (q, *J* = 6.6 Hz, 1H), 3.67 (t, *J* = 7.8 Hz, 2H), 3.01 (t, *J* = 7.8 Hz, 2H), 2.54 (t, *J* = 7.8 Hz, 2H), 2.35 (t, *J* = 7.8 Hz, 2H), 1.62 (d, *J* = 6.6 Hz, 3H), 0.89 (s, 9H), 0.06 (s, 6H); ¹³C NMR (150 MHz, CDCl₃) 171.2, 135.6, 135.1, 130.3, 125.1, 124.6, 123.6, 121.8, 120.8, 116.6, 109.0, 61.8, 35.0, 33.8, 32.2, 25.9, 18.3, 13.5, -5.3; HRMS Calcd. for C₂₂H₃₄NO₂Si [M⁺+H] 372.2359, found 372.2350.

1-(1*H*-Indol-1-yl)-4-phenylbutan-1-one (10j)

According to the general procedure described for **10a**, *N*-acylindole **10j** (112 mg, 0.426 mmol, 89%) was obtained from 4-phenylbutyric acid (**9j**) (79.0 mg, 0.478 mmol) and indole (**1**) (141 mg, 1.20 mmol); a white solid; Mp 47-49 °C (hexanes-AcOEt); IR (neat) 2953, 1705, 1452, 1386, 1339, 1308, 1205, 767, 750, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 7.8 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 7.37–7.29 (m, 4H), 7.26 (dd, *J* = 8.4, 7.8 Hz, 1H), 7.23–7.20 (m, 3H), 6.61 (d, *J* = 4.2 Hz, 1H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.79 (t, *J* = 7.2 Hz, 2H), 2.19 (tt, *J* = 7.2, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 171.2, 141.2, 135.6, 130.3, 128.5, 126.1, 125.1, 124.5, 123.6, 120.8, 116.6, 109.0, 35.0, 34.8, 26.0 (One

signal is missing due to overlap); HRMS Calcd. for $C_{18}H_{18}NO$ [M⁺+H] 264.1388, found 264.1364.

3-(2-Bromophenyl)-1-(1H-indol-1-yl)propan-1-one (10k)

According to the general procedure described for **10a**, *N*-acylindole **10k** (106 mg, 0.325 mmol, 87%) was obtained from 3-(2-bromophenyl)propionic acid (**9k**) (86.0 mg, 0.376 mmol) and indole (**1**) (110 mg, 0.939 mmol); a white solid; Mp 88-90 °C (hexanes-AcOEt); IR (neat) 2948, 1706, 1451, 1327, 1205, 767, 748 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.48 (d, *J* = 7.8 Hz, 1H), 7.51–7.55 (m, 2H), 7.46 (d, *J* = 3.6 Hz, 1H), 7.37–7.34 (m, 2H), 7.29–7.24 (m, 2H), 7.11 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.62 (d, *J* = 3.6 Hz, 1H), 3.30–3.23 (m, 4H); ¹³C NMR (150 MHz, CDCl₃) δ 170.3, 139.6, 135.6, 133.0, 130.9, 130.3, 128.3, 127.8, 125.2, 124.5, 124.3, 123.7, 120.8, 116.6, 109.3, 35.9, 31.3; HRMS Calcd. for C₁₇H₁₅BrNO [M⁺+H] 328.0337, found 328.0316.

3-(3-Bromophenyl)-1-(1*H*-indol-1-yl)propan-1-one (10l)

According to the general procedure described for 10a, *N*-acylindole 101 (87.5 mg, 0.268 mmol, 85%) was obtained from 3-(3-bromophenyl)propionic acid (91) (72.0 mg, 0.315 mmol) and indole (1) (92.0 mg, 0.785 mmol); a white solid; Mp 59-61 °C (hexanes-AcOEt); IR (neat) 2953, 1707, 1452, 1326, 1205, 767, 751 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.44 (s, 1H), 7.42 (d, *J* = 4.2 Hz, 1H), 7.37–7.35 (m, 2H), 7.29–7.17 (m, 3H), 6.63 (d, *J* = 4.2 Hz, 1H), 3.22 (t, *J* = 7.8 Hz, 2H), 3.14 (t, *J* = 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 170.0, 142.7, 135.6, 131.5, 130.3, 130.2, 129.6, 127.2, 125.2, 124.3, 123.7, 122.6, 120.9, 116.6, 109.4, 37.3, 30.0; HRMS Calcd. for C₁₇H₁₅BrNO [M⁺+H] 328.0337, found 328.0320.

4-(3-(1*H*-Indol-1-yl)-3-oxopropyl)benzonitrile (10m)

According to the general procedure described for **10a**, *N*-acylindole **10m** (70.8 mg, 0.258 mmol, 78%) was obtained from 3-(4-cyanophenyl)propionic acid (**9m**) (58.0 mg, 0.330 mmol) and indole (**1**) (97.0 mg, 0.828 mmol); a white solid; Mp 121-122 °C (hexanes-AcOEt); IR (neat) 2953, 2226, 1705, 1452, 1389, 1328, 1206, 767, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.44–7.42 (m, 4H), 7.29–7.17 (m, 3H), 6.63 (d, *J* = 4.2 Hz, 1H), 3.22 (t, *J* = 7.8 Hz, 2H), 3.14 (t, *J* = 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 169.7, 146.0, 135.6, 132.4, 130.3, 129.3, 125.3, 124.1, 123.8, 120.9, 118.8, 116.5, 110.4, 109.6, 36.7, 30.3; HRMS Calcd. for C₁₈H₁₅N₂O [M⁺+H] 275.1184, found 275.1170.

1-(1*H*-Indol-1-yl)-3-(4-nitrophenyl)propan-1-one (10n)

According to the general procedure described for **10a**, *N*-acylindole **10n** (84.9 mg, 0.289 mmol, 76%) was obtained from 3-(4-nitrophenyl)propionic acid (**9n**) (75.0 mg, 0.387 mmol) and indole (**1**) (113 mg, 0.964 mmol); a white solid; Mp 149-151 °C (hexanes-AcOEt); IR (neat) 2953, 1707, 1509, 1453, 1345, 1333, 1206, 1112, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.44 (d, *J* = 7.8 Hz, 1H), 8.17 (d, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 9.0 Hz, 2H), 7.57 Hz, 1H), 6.65 (d, *J* = 3.6 Hz, 1H), 7.28 (dd, *J* = 7.8, 7.5 Hz, 1H), 6.65 (d, *J* = 3.6 Hz, 1H), 3.29 (s, 4H); ¹³C NMR (150 MHz, CDCl₃) δ 169.6, 148.1, 146.7, 135.6, 130.3, 129.4, 125.3, 124.1, 123.9, 121.0, 116.5, 109.7, 36.6, 30.0 (One signal is missing due to overlap); HRMS Calcd. for C₁₇H₁₅N₂O₃ [M⁺+H] 295.1083, found 295.1077.

Methyl 4-(3-(1*H*-indol-1-yl)-3-oxopropyl)-3-nitrobenzoate (10o)

According to the general procedure described for **10a**, *N*-acylindole **10o** (81.4 mg, 0.231 mmol, 72%) was obtained from **9o** (81.0 mg, 0.321 mmol) and indole (**1**) (94.0 mg, 0.802 mmol); a white solid; Mp 155-157 °C (hexanes-AcOEt); IR (neat) 2949, 1716, 1536, 1453, 1319, 1261, 764 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.62 (s, 1H), 8.44 (d, *J* = 7.8 Hz, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.44 (d, *J* = 3.6 Hz, 1H), 7.36 (dd, *J* = 8.1, 7.8 Hz, 1H), 7.28 (dd, *J* = 8.4, 8.1 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 1H), 3.96 (s, 3H), 3.48 (t, *J* = 7.2 Hz, 2H), 3.37 (t, *J* = 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 169.6, 164.8, 149.3, 140.3, 135.6, 133.8, 133.1, 130.3, 130.2, 126.2, 125.3, 124.2, 123.8, 120.9, 116.5, 109.6, 52.7, 36.3, 28.3; HRMS Calcd. for C₁₉H₁₆N₂NaO₅ [M+Na⁺] 375.0957, found 375.0939.

1-(1*H*-Indol-1-yl)-3-(6-nitrobenzo[*d*][1,3]dioxol-5yl)propan-1-one (10p)

According to the general procedure described for **10a**, *N*-acylindole **10p** (103 mg, 0.302 mmol, 70%) was obtained from **9p** (103 mg, 0.431 mmol) and indole (**1**) (127 mg, 1.08 mmol); a white solid; Mp 147-148 °C (hexanes-AcOEt); IR (neat) 2949, 1704, 1519, 1327, 1256, 1206, 1037, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.46 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.4 Hz, 1H), 7.54 (s, 1H), 7.48 (d, *J* = 3.6 Hz, 1H), 7.36 (dd, *J* = 8.4, 7.2 Hz, 1H), 7.27 (dd, *J* = 8.4, 7.2 Hz, 1H), 6.63 (d, *J* = 3.6 Hz, 1H), 6.09 (s, 2H), 3.38 (t, *J* = 7.2 Hz, 2H), 3.33 (t, *J* = 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 170.2, 152.0, 146.9, 142.8, 135.6, 133.0, 130.4, 125.2, 124.5, 123.7, 120.9, 116.6, 111.4, 109.4, 105.8, 102.9, 36.6, 29.2; HRMS Calcd. for C₁₈H₁₅N₂O₅ [M⁺+H] 339.0981, found 339.0984.

1-(1*H*-Indol-1-yl)-3-(thiophen-2-yl)propan-1-one (10q)

According to the general procedure described for 10a, *N*-acylindole 10q (51.3 mg, 0.201 mmol, 82%) was obtained from 3-(2-thienyl)propionic acid (9q) (38.0 mg, 0.244 mmol) and indole (1) (71.0 mg, 0.606 mmol); a white solid; Mp 65-66 °C (hexanes-AcOEt); IR (neat) 2953, 1705, 1452, 1324, 1205, 767, 751, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.47 (d, *J* = 7.8 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 3.0 Hz, 1H), 7.36 (dd, *J* = 7.8, 7.5 Hz, 1H), 7.27 (dd, *J* = 7.5, 7.2 Hz, 1H), 7.15 (d, *J* = 4.8 Hz, 1H), 6.93 (dd, *J* = 4.8, 4.2 Hz, 1H), 6.91 (d, *J* = 4.2 Hz, 1H), 6.63 (d, *J* = 3.0 Hz, 1H), 3.29 (t, *J* = 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 170.0, 142.8, 135.6, 130.3, 127.0, 125.2, 125.0, 124.3, 123.7, 120.9, 116.6, 109.4, 37.8, 24.6 (One signal is missing due to overlap); HRMS Calcd. for C₁₅H₁₄NOS [M⁺+H] 256.0796, found 256.0785.

1-(1*H*-Indol-1-yl)-2-(1,4-dioxaspiro[4.5]decan-8yl)ethanone (10r)

According to the general procedure described for **10a**, *N*-acylindole **10r** (52.5 mg, 0.175 mmol, 56%) was obtained from **9r** (63.0 mg, 0.315 mmol) and indole (**1**) (92.0 mg, 0.788 mmol); a white solid; Mp 96-98 °C (hexanes-AcOEt); IR (neat) 2953, 1704, 1452, 1317, 1204, 1105, 752 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.48 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.35 (dd, *J* = 8.4, 7.8 Hz, 1H), 7.21 (dd, *J* = 7.8, 7.8 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 3.95 (s, 4H), 2.82 (d, *J* = 7.2 Hz, 2H), 2.15–2.08 (m, 1H),

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- 1.90–1.88 (m, 2H), 1.78–1.76 (m, 2H), 1.65–1.59 (m, 2H), 1.45–1.39 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 170.7, 135.6, 130.4, 125.1, 124.7, 123.6, 120.8, 116.7, 109.0, 108.5,
- 64.3, 64.2, 42.2, 34.3, 33.3, 30.2; HRMS Calcd. for
- $C_{18}H_{22}NO_3$ [M⁺+H] 300.1600, found 300.1579.

Cyclopent-3-en-1-yl(1*H*-indol-1-yl)methanone (10s)

According to the general procedure described for 10a, Nacylindole 10s (46.7 mg, 0.221 mmol, 76%) was obtained from 3-cyclopentenecarboxylic acid (9s) (33.0 mg, 0.291 mmol) and indole (1) (85.0 mg, 0.725 mmol); a white solid; Mp 76-77 °C (hexanes-AcOEt); IR (neat) 2953, 1700, 1451, 1360, 1339, 1309, 1289, 1224, 1206, 767, 750, 717 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.51 (d, J = 7.8 Hz, 1H), 7.57 (d, J = 7.2 Hz, 1H), 7.49 (d, J = 4.2 Hz, 1H), 7.35 (dd, J = 7.8, 7.5 18 Hz, 1H), 7.27 (dd, J = 7.5, 7.2 Hz, 1H), 6.65 (d, J = 4.2 Hz, 19 1H), 5.74 (s, 2H), 3.85 (tt, J = 9.6, 6.0 Hz, 1H), 2.93 (dd, J =14.7, 6.0 Hz, 2H), 2.81 (dd, J = 14.7, 9.6 Hz, 2H); ¹³C NMR 20 (150 MHz, CDCl₃) δ 174.0, 135.9, 130.3, 128.8, 125.1, 124.7, 21 123.6, 120.7, 116.8, 109.1, 42.0, 36.9; HRMS Calcd. for 22 C₁₄H₁₄NO [M⁺+H] 212.1075, found 212.1060. 23

(S)-Benzyl 2-(1*H*-indole-1-carbonyl)pyrrolidine-1carboxylate (10t)

According to the general procedure described for 10a, Nacylindole 10t (101 mg, 0.292 mmol, 72%, >99% ee) was obtained from Cbz-L-proline 9t (101 mg, 0.405 mmol) and indole (1) (118 mg, 1.01 mmol) in the presence of DMAP (10 mg, 0.082 mmol), and 2,6-lutidine (14 μ L, 0.12 mmol); a white solid; Mp 31-32 °C (hexanes-AcOEt); Enantiomeric excess was determined by HPLC analysis (CHIRALCEL OJ-H column, n-hexane-isopropanol (80:20 v/v as an eluent), 0.8 mL/min, $\lambda = 254$ nm, 25 °C, the retention times of (+)-isomer and (-)-isomer are 27 min and 50 min, respectively); $\left[\alpha\right]_{D}^{26}$ -109.3 (c 0.81, CHCl₃); IR (neat) 2954, 1700, 1452, 1415, 1355, 1308, 1204, 1123, 765, 751 cm⁻¹; ¹H NMR (600 MHz, CDCl₃, a mixture of two rotamers) δ 8.48–8.45 (m, 1H), 7.58– 7.26 (m, 7H), 7.12-7.00 (m, 2H), 6.68-6.62 (m, 1H), 5.23-5.01 (m, 3H), 3.81-3.79 (m, 1H), 3.68-3.59 (m, 1H), 2.44-2.38 (m, 1H), 2.15–2.10 (m, 2H), 2.01–2.00 (m, 1H); ¹³C NMR (150 MHz, CDCl₃, a mixture of two rotamers) δ 170.7, 170.4, 155.0, 154.1, 136.6, 136.2, 135.94, 135.88, 128.5, 128.2, 128.0, 127.9, 127.7, 127.6, 125.4, 125.2, 124.0, 123.9, 123.6, 120.84, 120.80, 116.9, 116.8, 109.8, 67.23, 67.19, 59.5, 59.0, 47.2, 46.6, 31.4, 30.4, 24.3, 23.5; HRMS Calcd. for C₂₁H₂₀N₂NaO₃ [M+Na⁺] 371.1372, found 371.1354.

(1*H*-Indol-1-yl)(phenyl)methanone (10u)

According to the general procedure described for **10a**, *N*-acylindole **10u** (31.0 mg, 0.140 mmol, 42%) was obtained from benzoic acid (**9u**) (41.0 mg, 0.337 mmol) and indole (**1**) (99.0 mg, 0.844 mmol) in the presence of DMAP (8.20 mg, 0.0674 mmol), and 2,6-lutidine (12 μ L, 0.10 mmol); a white solid; Mp 61-62 °C (hexanes-AcOEt); IR (neat) 2949, 1686, 1450, 1340, 1205, 887, 750, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.40 (d, *J* = 7.8 Hz, 1H), 7.74 (d, *J* = 7.2 Hz, 2H), 7.65–7.60 (m, 2H), 7.53 (dd, *J* = 8.1, 7.2 Hz, 2H), 7.39 (dd, *J* = 8.1, 7.8 Hz, 1H), 7.33–7.30 (m, 2H), 6.62 (d, *J* = 3.6 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) δ 168.7, 136.0, 134.6, 131.9, 130.8, 129.1, 128.6, 127.6, 124.9, 123.9, 120.9, 116.4, 108.5; HRMS Calcd. for C₁₅H₁₂NO [M⁺+H] 222.0919, found

222.0913. Spectroscopic date matched those previously reported. $^{\rm 3h}$

(1H-Indol-1-yl)(pyridin-2-yl)methanone (10v)

According to the general procedure described for 10a, Nacylindole 10v (73.3 mg, 0.330 mmol, 98%) was obtained from 2-pyridinecarboxylic acid (9v) (42.0 mg, 0.337 mmol) and indole (1) (99.0 mg, 0.844 mmol) in the presence of DMAP (8.20 mg, 0.0674 mmol), and 2,6-lutidine (12 µL, 0.10 mmol); a white solid; Mp 79-81 °C (hexanes-AcOEt); IR (neat) 2949, 1684, 1539, 1451, 1437, 1382, 1347, 1205, 1193, 890, 767, 747, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.74 (dd, J = 4.8, 1.2 Hz, 1H), 8.54 (d, J = 7.8 Hz, 1H), 8.09 (d, J =7.2 Hz, 1H), 7.98 (d, J = 4.2 Hz, 1H), 7.94 (ddd, J = 7.5, 7.2, 1.2 Hz, 1H), 7.59 (d, J = 7.2 Hz, 1H), 7.51 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 7.39 (dd, J = 7.8, 7.5 Hz, 1H), 7.32 (dd, J = 7.5, 7.2 Hz, 1H), 6.64 (d, J = 4.2 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) & 165.7, 152.4, 148.5, 137.4, 136.4, 130.7, 128.4, 126.1, 125.7, 124.9, 124.1, 120.7, 116.9, 109.1; HRMS Calcd. $C_{14}H_{11}N_{2}O$ [M⁺+H] 223.0871, found 223.0869. for Spectroscopic date matched those previously reported.^{3h}

(1H-Indol-1-yl)(quinolin-2-yl)methanone (10w)

According to the general procedure described for 10a, Nacylindole 10w (78.3 mg, 0.288 mmol, 70%) was obtained from 2-quinolinecarboxylic acid (9w) (71.0 mg, 0.411 mmol) and indole (1) (121 mg, 1.03 mmol) in the presence of DMAP (10.0 mg, 0.0819 mmol), and 2,6-lutidine (14 µL, 0.12 mmol); a white solid; Mp 125-127 °C (hexanes-AcOEt); IR (neat) 2953, 1684, 1451, 1383, 1349, 1206, 902, 825, 771, 761, 749 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.60 (d, J = 8.4 Hz, 1H), 8.39 (d. J = 8.4 Hz, 1H), 8.22 (d. J = 8.4 Hz, 1H), 8.16 (d. J =4.2 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.4 Hz, 1H), 7.83 (dd, J = 8.4, 7.5 Hz, 1H), 7.70 (dd, J = 8.4, 7.5 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.41 (dd, J = 8.4, 7.2 Hz, 1H), 7.33 (d, J = 7.8, 7.2 Hz, 1H), 6.66 (d, J = 4.2 Hz, 1H); ¹³C NMR (150 MHz, CDCl₃) & 165.9, 151.9, 146.6, 137.5, 136.5, 130.8, 130.5, 130.3, 128.7, 128.6, 127.7, 125.0, 124.2, 121.6, 120.7, 117.0, 109.2 (One signal is missing due to overlap); HRMS Calcd. for $C_{18}H_{13}N_2O[M^++H]$ 273.1028, found 273.1021.

1-(6-Bromo-1*H*-indol-1-yl)-4-phenylbutan-1-one (12a)

According to the general procedure described for **10a**, *N*-acylindole **12a** (80.6 mg, 0.236 mmol, 88%) was obtained from 4-phenylbutyric acid (**9j**) (44.0 mg, 0.268 mmol) and 6-bromoindole (**11a**) (131 mg, 0.668 mmol); a white solid; Mp 93-94 °C (hexanes-AcOEt); IR (neat) 2953, 1713, 1449, 1428, 1301, 1200, 886, 699 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.69 (s, 1H), 7.41–7.37 (m, 2H), 7.33–7.29 (m, 3H), 7.22–7.20 (m, 3H), 6.57 (d, *J* = 3.6 Hz, 1H), 2.88 (t, *J* = 7.8 Hz, 2H), 2.79 (t, *J* = 7.8 Hz, 2H), 2.18 (tt, *J* = 7.8, 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 171.1, 141.0, 136.2, 129.0, 128.53, 128.48, 126.9, 126.2, 124.9, 121.8, 119.7, 118.8, 108.7, 34.9, 34.7, 25.8; HRMS Calcd. for C₁₈H₁₇BrNO [M⁺+H] 342.0494, found 342.0474.

1-(4-Phenylbutanoyl)-1*H*-indole-5-carbaldehyde (12b)

According to the general procedure described for 10a, *N*-acylindole 12b (65.5 mg, 0.225 mmol, 84%) was obtained from 4-phenylbutyric acid (9j) (44.0 mg, 0.268 mmol) and indole-5-carbaldehyde (11b) (97.0 mg, 0.668 mmol); a white solid; Mp 69-70 °C (hexanes-AcOEt); IR (neat) 2974, 1715, 1691, 1381, 1308, 1194, 1156, 700 cm⁻¹; ¹H NMR (600 MHz,

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CDCl₃) δ 10.1 (s, 1H), 8.60 (d, J = 7.8 Hz, 1H), 8.10 (s, 1H), 7.89 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 3.6 Hz, 1H), 7.33–7.30 (m, 2H), 7.23–7.21 (m, 3H), 6.73 (d, J = 3.6 Hz, 1H), 2.93 (t, J= 7.2 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 2.20 (tt, J = 7.2, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 192.0, 171.3, 140.9, 139.0, 132.4, 130.5, 128.6, 128.5, 126.33, 126.29, 126.23, 123.6, 117.0, 109.4, 34.88, 34.85, 25.8; HRMS Calcd. for C₁₉H₁₈NO₂ [M⁺+H] 292.1338, found 292.1320.

1-(5-Nitro-1*H*-indol-1-yl)-4-phenylbutan-1-one (12c)

According to the general procedure described for **10a**, *N*-acylindole **12c** (77.3 mg, 0.251 mmol, 93%) was obtained from 4-phenylbutyric acid (**9j**) (45.0 mg, 0.271 mmol) and 5-nitroindole (**11c**) (110 mg, 0.678 mmol); a pale yellow solid; Mp 89-90 °C (hexanes-AcOEt); IR (neat) 2974, 1717, 1518, 1339, 1308, 1198, 770, 742 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.58 (d, *J* = 8.4 Hz, 1H), 8.47 (s, 1H), 8.23 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 3.6 Hz, 1H), 2.94 (t, *J* = 7.2 Hz, 2H), 2.81 (t, *J* = 6.6 Hz, 2H), 2.21 (tt, *J* = 7.2, 6.6 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 171.3, 144.2, 140.8, 138.5, 130.1, 128.6, 128.5, 127.4, 126.3, 120.3, 117.0, 116.8, 109.4, 34.80, 34.77, 25.7; HRMS Calcd. for C₁₈H₁₆N₂NaO₃ [M+Na⁺] 331.1059, found 331.1032.

1-(4-Phenylbutanoyl)-1*H*-indole-3-carbaldehyde (12d)

According to the general procedure described for **10a**, *N*-acylindole **12d** (97.8 mg, 0.336 mmol, 96%) was obtained from 4-phenylbutyric acid (**9j**) (57.0 mg, 0.350 mmol) and indole-3-carbaldehyde (**11d**) (127 mg, 0.875 mmol); a white solid; Mp 87-88 °C (hexanes-AcOEt); IR (neat) 2973, 1727, 1676, 1550, 1447, 1187, 1126, 752, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 10.1 (s, 1H), 8.41 (d, *J* = 8.4 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.94 (s, 1H), 7.34–7.31 (m, 2H), 7.26–7.22 (m, 3H), 2.97 (t, *J* = 7.8 Hz, 2H), 2.81 (t, *J* = 7.8 Hz, 2H), 2.22 (tt, *J* = 7.8, 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 185.6, 171.2, 140.7, 136.4, 134.5, 128.6, 128.5, 126.8, 126.4, 125.9, 125.3, 122.5, 121.9, 116.4, 34.7, 34.6, 25.7; HRMS Calcd. for C₁₉H₁₈NO₂ [M⁺+H] 292.1338, found 292.1318.

1-(3-Acetyl-1*H*-indol-1-yl)-4-phenylbutan-1-one (12e)

According to the general procedure described for 10a, N-42 acylindole 12e (92.6 mg, 0.303 mmol, 97%) was obtained 43 from 4-phenylbutyric acid (9j) (51.0 mg, 0.313 mmol) and 3-44 acetylindole (11e) (125 mg, 0.785 mmol); a white solid; Mp 45 101-103 °C (hexanes-AcOEt); IR (neat) 2949, 1718, 1665, 46 1545, 1448, 1388, 1197, 1148, 1016, 753 cm⁻¹; ¹H NMR (600 47 MHz, CDCl₃) δ 8.38 (d, J = 7.8 Hz, 1H), 8.33 (d, J = 7.2 Hz, 48 1H), 7.93 (s, 1H), 7.42–7.37 (m, 2H), 7.34–7.31 (m, 2H), 49 7.26–7.22 (m, 3H), 2.96 (t, J = 7.8 Hz, 2H), 2.82 (t, J = 7.850 Hz, 2H), 2.53 (s, 3H), 2.22 (tt, J = 7.8, 7.8 Hz, 2H); ¹³C NMR 51 (150 MHz, CDCl₃) & 193.7, 171.3, 140.8, 136.0, 130.5, 128.6, 52 128.5, 127.1, 126.3, 126.2, 125.1, 122.4, 121.8, 116.2, 34.75, 53 34.71, 27.9, 25.8; HRMS Calcd. for $C_{20}H_{20}NO_2$ [M⁺+H] 306.1494. found 306.1483. 54

Ethyl 1-(4-phenylbutanoyl)-1*H*-indole-2-carboxylate (12f) According to the general procedure described for 10a, *N*acylindole 12f (101 mg, 0.300 mmol, 91%) was obtained from 4-phenylbutyric acid (9j) (54.0 mg, 0.330 mmol) and ethyl indole-2-carboxylate (11f) (156 mg, 0.824 mmol); a colorless oil; IR (neat) 2949, 1720, 1536, 1444, 1377, 1202, 747, 700

cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.00 (d, J = 8.4 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.42 (dd, J = 8.4, 6.6 Hz, 1H), 7.31 (s, 1H), 7.28–7.23 (m, 3H), 7.18–7.12 (m, 3H), 4.34 (q, J =7.8 Hz, 2H), 2.87 (t, J = 7.8 Hz, 2H), 2.66 (t, J = 7.8 Hz, 2H), 2.11 (tt, J = 7.8, 7.8 Hz, 2H), 1.37 (t, J = 7.8 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 174.3, 161.7, 141.2, 138.2, 129.5, 128.42, 128.39, 127.7, 127.2, 126.0, 123.5, 122.4, 117.6, 114.7, 61.6, 38.9, 35.0, 27.0, 14.2; HRMS Calcd. for C₂₁H₂₁NNaO₃ [M+Na⁺] 358.1419, found 358.1409.

1-(2-Iodo-1*H*-indol-1-yl)-4-phenylbutan-1-one (12g)

According to the general procedure described for **10a**, *N*-acylindole **12g** (130 mg, 0.333 mmol, 90%) was obtained from 4-phenylbutyric acid (**9j**) (61.0 mg, 0.370 mmol) and 2-iodoindole (**11g**)¹³ (225 mg, 0.926 mmol); a pale yellow solid; Mp 49-50 °C (hexanes-AcOEt); IR (neat) 2949, 1711, 1438, 1259, 746 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.94 (d, *J* = 7.2 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 1H), 7.30–7.19 (m, 7H), 7.02 (s, 1H) 3.18 (t, *J* = 7.2 Hz, 2H), 2.77 (t, *J* = 7.8 Hz, 2H), 2.19 (tt, *J* = 7.8, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 173.0, 141.1, 137.8, 131.1, 128.53, 128.48, 126.1, 124.7, 123.4, 123.2, 119.6, 114.8, 73.2, 39.2, 35.0, 26.9; HRMS Calcd. for C₁₈H₁₆INNaO [M+Na⁺] 412.0174, found 412.0167.

4-Phenyl-1-(2-phenyl-1*H*-indol-1-yl)butan-1-one (12h)

According to the general procedure described for 10a, *N*-acylindole 12h (35.3 mg, 0.104 mmol, 33%) was obtained from 4-phenylbutyric acid (9j) (52.0 mg, 0.320 mmol) and 2-phenylindole (11h) (154 mg, 0.798 mmol); a colorless oil; IR (neat) 2929, 1703, 1451, 1370, 1329, 1283, 1268, 1164, 749, 699 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.30 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 7.2 Hz, 1H), 7.56–7.39 (m, 5H), 7.36–7.26 (m, 2H), 7.19–7.12 (m, 3H), 6.90 (d, *J* = 6.6 Hz, 2H), 6.60 (s, 1H), 2.38 (t, *J* = 7.8 Hz, 2H), 2.26 (t, *J* = 7.8 Hz, 2H), 1.87 (tt, *J* = 7.8, 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 174.7, 141.0, 139.4, 137.6, 134.2, 129.0, 128.71, 128.69, 128.5, 128.34, 128.28, 125.8, 125.0, 123.5, 120.4, 115.6, 111.3, 39.1, 34.8, 26.8; HRMS Calcd. for C₂₄H₂₂NO [M⁺+H] 340.1701, found 340.1683.

1-(2-(4-((*tert*-Butyldiphenylsilyl)oxy)but-1-yn-1-yl)-1*H*-indol-1-yl)-4-phenylbutan-1-one (12i)

According to the general procedure described for **10a**, *N*-acylindole **12i** (234 mg, 0.411 mmol, 98%) was obtained from 4-phenylbutyric acid (**9j**) (69.0 mg, 0.418 mmol) and indole **11i** (440 mg, 1.04 mmol); a pale yellow solid; Mp 73-75 °C (hexanes-AcOEt); IR (neat) 2950, 1707, 1449, 1284, 1110, 742, 701 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.43 (d, *J* = 8.4 Hz, 1H), 7.70–7.68 (m, 4H), 7.47–7.33 (m, 8H), 7.26–7.23 (m, 3H), 7.17–7.14 (m, 3H), 6.81 (s, 1H), 3.85 (t, *J* = 6.6 Hz, 2H), 3.22 (t, *J* = 7.2 Hz, 2H), 2.68–2.66 (m, 4H), 2.11 (tt, *J* = 7.2, 6.6 Hz, 2H), 1.08 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 173.3, 141.5, 136.5, 135.6, 133.4, 129.8, 128.6, 128.44, 128.37, 127.7, 125.99, 125.97, 123.8, 120.2, 119.7, 117.5, 117.0, 95.9, 74.7, 61.9, 37.3, 35.1, 26.8, 26.4, 24.0, 19.2; HRMS Calcd. for C₃₈H₄₀NO₂Si [M⁺+H] 570.2828, found 570.2785.

1-(7-(Benzyloxy)-1*H***-indol-1-yl)-4-phenylbutan-1-one (12j)** According to the general procedure described for **10a**, *N*-acylindole **12j** (80.9 mg, 0.218 mmol, 93%) was obtained from 4-phenylbutyric acid (**9j**) (39.0 mg, 0.236 mmol) and 7benzyloxyindole (**11j**) (132 mg, 0.592 mmol); a pale yellow

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solid; Mp 42-43 °C (hexanes-AcOEt); IR (neat) 2953, 1726, 1704, 1583, 1485, 1421, 1300, 1260, 1247, 1196, 1070, 788, 742, 722, 697 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.54 (d, J = 3.6 Hz, 1H), 7.45 (d, J = 7.8 Hz, 2H), 7.38–7.31 (m, 3H), 7.25–7.14 (m, 5H), 7.56 (d, J = 7.2 Hz, 2H), 6.89 (d, J = 7.8 Hz, 1H), 6.57 (d, J = 3.6 Hz, 1H), 5.18 (s, 2H), 2.95 (t, J = 7.8 Hz, 2H), 1.98 (tt, J = 7.8 Hz, 2H), ¹³C NMR (150 MHz, CDCl₃) δ 172.9, 147.2, 141.4, 136.5, 134.2, 128.6, 128.4, 128.3, 128.1, 127.7, 127.5, 125.9, 124.7, 124.0, 114.2, 108.0, 107.6, 71.1, 37.3, 34.9, 27.0; HRMS Calcd. for C₂₅H₂₄NO₂ [M⁺+H] 370.1807, found 370.1798.

Ethyl 1-(4-phenylbutanoyl)-1*H*-pyrrole-2-carboxylate (12k)

According to the general procedure described for 10a, Nacylpyrrole 12k (65.3 mg, 0.229 mmol, 68%) was obtained from 4-phenylbutyric acid (9i) (55.0 mg, 0.335 mmol) and ethyl pyrrole-2-carboxylate (11k) (117 mg, 0.841 mmol); a colorless oil; IR (neat) 2978, 1717, 1453, 1416, 1270, 1245, 1209, 1108, 756, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.29–7.26 (m, 2H), 7.23 (dd, J = 2.4, 1.2 Hz, 1H), 7.21–7.17 24 (m, 3H), 6.93 (dd, J = 3.6, 1.2 Hz, 1H), 6.20 (dd, J = 3.6, 2.4 25 Hz, 1H), 4.29 (q, J = 7.8 Hz, 2H), 2.88 (t, J = 7.8 Hz, 2H), 26 2.71 (t, J = 7.8 Hz, 2H), 2.10 (tt, J = 7.8, 7.8 Hz, 2H), 1.34 (t, 27 J = 7.8 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 172.2, 161.2, 28 141.1, 128.4, 126.1, 125.5, 125.2, 122.0, 110.8, 61.0, 36.2, 29 34.8, 26.4, 14.2 (One signal is missing due to overlap); HRMS 30 Calcd. for $C_{17}H_{19}NNaO_3$ [M+Na⁺] 308.1263, found 308.1265.

1-(2-acetyl-1*H*-pyrrol-1-yl)-4-phenylbutan-1-one (12l)

32 According to the general procedure described for 10a. N-33 acylpyrrole 12l (60.0 mg, 0.235 mmol, 78%) was obtained 34 from 4-phenylbutyric acid (9i) (49.0 mg, 0.300 mmol) and 2-35 acecyl pyrrole (111) (81.0 mg, 0.750 mmol); a colorless oil; IR (neat) 2929, 1735, 1661, 1433, 1411, 1266, 747, 700 cm⁻¹; ¹H 36 NMR (400 MHz, CDCl₃) δ 7.29–7.14 (m, 6H), 6.98 (dd, J = 37 3.4, 1.6 Hz, 1H), 6.22 (dd, J = 3.4, 2.8 Hz, 1H), 2.81 (t, J = 7.238 Hz, 2H), 2.69 (t, J = 7.6 Hz, 2H), 2.44 (s, 3H), 2.08 (tt, J = 39 7.6, 7.2 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 188.5, 174.1, 40 141.1, 133.7, 128.41, 128.36, 127.6, 126.0, 122.9, 110.5, 37.3, 41 34.8, 27.2, 26.6; HRMS Calcd. for $C_{16}H_{17}NNaO_2$ [M+Na⁺] 42 278.1157, found 278.1146. 43

4-Phenyl-1-(1*H*-pyrazol-1-yl)butan-1-one (12m)

According to the general procedure described for **10a**, *N*-acylpyrazole **12m** (59.2 mg, 0.276 mmol, 85%) was obtained from 4-phenylbutyric acid (**9j**) (53.0 mg, 0.324 mmol) and pyrazole (**11m**) (55.0 mg, 0.808 mmol); a white solid; Mp 34-35 °C (hexanes-AcOEt); IR (neat) 2978, 1735, 1415, 1344, 1200, 923, 745, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.25 (d, *J* = 3.0 Hz, 1H), 7.69 (d, *J* = 1.8 Hz, 1H), 7.31–7.18 (m, 5H), 6.43 (dd, *J* = 3.0, 1.8 Hz, 1H), 3.17 (t, *J* = 7.8 Hz, 2H), 2.75 (t, *J* = 7.8 Hz, 2H), 2.13 (tt, *J* = 7.8, 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 172.0, 143.9, 141.3, 128.5, 128.4, 128.2, 126.0, 109.5, 35.1, 33.3, 25.9; HRMS Calcd. for C₁₃H₁₄N₂NaO [M+Na⁺] 237.1004, found 237.0987.

56 1-(9*H*-Carbazol-9-yl)-4-phenylbutan-1-one (12n)

According to the general procedure described for **10a**, *N*-acylcarbazole **12n** (85.3 mg, 0.272 mmol, 87%) was obtained from 4-phenylbutyric acid (**9j**) (51.0 mg, 0.313 mmol) and carbazole (**11n**) (131 mg, 0.783 mmol); a white solid; Mp 87-

88 °C (hexanes-AcOEt); IR (neat) 2949, 1696, 1445, 1375, 1283, 1210, 1156, 753, 721 cm⁻¹, ¹H NMR (600 MHz, CDCl₃) δ 8.14 (d, *J* = 7.8 Hz, 2H), 7.98 (d, *J* = 7.8 Hz, 2H), 7.44 (dd, *J* = 7.8, 7.5 Hz, 2H), 7.37 (dd, *J* = 7.8, 7.5 Hz, 2H), 7.31 (dd, *J* = 7.5, 7.2 Hz, 2H), 7.26–7.20 (m, 3H), 3.13 (t, *J* = 7.8 Hz, 2H), 2.84 (t, *J* = 7.8 Hz, 2H), 2.27 (tt, *J* = 7.8, 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 173.0, 141.4, 138.5, 128.6, 128.5, 127.3, 126.4, 126.1, 123.5, 119.8, 116.4, 38.3, 35.1, 26.3; HRMS Calcd. for C₂₂H₂₀NO [M⁺+H] 314.1545, found 314.1534.

1-(4-Phenylbutanoyl)pyrrolidin-2-one (14a)

According to the general procedure described for **10a**, imide **14a** (46.4 mg, 0.201 mmol, 64%) was obtained from 4phenylbutyric acid (**9j**) (51.0 mg, 0.313 mmol) and 2pyrrolidone (**13a**) (67.0 mg, 0.787 mmol); a white solid; Mp 55-56 °C (hexanes-AcOEt); IR (neat) 2953, 1738, 1692, 1362, 1252, 747, 701 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.29–7.17 (m, 5H), 3.79 (t, *J* = 7.8 Hz, 2H), 2.94 (t, *J* = 7.8 Hz, 2H), 2.69 (t, *J* = 7.2 Hz, 2H), 2.58 (t, *J* = 8.4 Hz, 2H), 2.04–1.96 (m, 4H); ¹³C NMR (150 MHz, CDCl₃) δ 175.3, 174.1, 141.8, 128.5, 128.3, 125.8, 45.4, 36.3, 35.2, 33.7, 25.8, 17.2; HRMS Calcd. for C₁₄H₁₇NNaO₂ [M+Na⁺] 254.1157, found 254.1153.

(*S*)-5-(((*tert*-Butyldimethylsilyl)oxy)methyl)-1-(4-phenylbutanoyl)pyrrolidin-2-one (14b)

According to the general procedure described for **10a**, imide **14b** (68.1 mg, 0.181 mmol, 41%) was obtained from 4phenylbutyric acid (**9j**) (72.0 mg, 0.440 mmol) and lactam **13b**¹⁴ (252 mg, 1.10 mmol); pale yellow oil; $[\alpha]_D^{27}$ –85.6 (*c* 1.00, CHCl₃); IR (neat) 2953, 1739, 1692, 1362, 1256, 1231, 1200, 1112, 837, 778 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.29–7.26 (m, 2H), 7.21–7.16 (m, 3H), 4.41–4.39 (m, 1H), 3.94 (dd, *J* = 10.5, 3.0 Hz, 1H), 3.65 (dd, *J* = 10.5, 2.4 Hz, 1H), 2.98–2.92 (m, 2H), 2.84–2.78 (m, 1H), 2.71–2.66 (m, 2H), 2.44–2.39 (m, 1H), 2.13–1.94 (m, 4H), 0.85 (s, 9H), 0.02 (s, 3H), -0.02 (s, 3H); ¹³C NMR (150 MHz, CDCl₃) δ 176.4, 174.0, 141.8, 128.5, 128.3, 125.8, 63.9, 58.0, 36.6, 35.3, 33.1, 25.9, 25.8, 21.2, 18.1, –5.6; HRMS Calcd. for C₂₁H₃₃NNaO₃Si [M+Na⁺] 398.2127, found 398.2112.

3-(4-Phenylbutanoyl)oxazolidin-2-one (14c)

According to the general procedure described for **10a**, imide **14c** (76.8 mg, 0.329 mmol, 91%) was obtained from 4phenylbutyric acid (**9j**) (59.0 mg, 0.361 mmol) and 2oxazolidone (**13c**) (79.0 mg, 0.907 mmol); a white solid; Mp 79-80 °C (hexanes-AcOEt); IR (neat) 2949, 1770, 1698, 1393, 1113, 1038, 758, 702 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.29–7.17 (m, 5H), 4.38 (t, *J* = 7.8 Hz, 2H), 3.98 (t, *J* = 7.8 Hz, 2H), 2.96 (t, *J* = 7.2 Hz, 2H), 2.69 (t, *J* = 7.2 Hz, 2H), 2.01 (tt, *J* = 7.2, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 173.2, 153.5, 141.5, 128.5, 128.3, 125.9, 62.0, 42.5, 35.1, 34.5, 25.8; HRMS Calcd. for C₁₃H₁₅NNaO₃ [M+Na⁺] 256.0950, found 256.0945.

(S)-4-Benzyl-3-(4-phenylbutanoyl)oxazolidin-2-one (14d)

According to the general procedure described for 10a, imide 14d (110 mg, 0.340 mmol, 98%) was obtained from 4phenylbutyric acid (9j) (57.0 mg, 0.348 mmol) and (S)-4benzyl-2-oxazolidinone (13d) (154 mg, 0.869 mmol). The reaction using equimolar amount of 13d with Boc₂O (1.5 eq) gave imide 14d in 80% yield; a white solid; Mp 78-80 °C (hexanes-AcOEt); $[\alpha]_D^{27}$ +50.2 (c 1.00, CHCl₃); IR (neat)

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2953, 1781, 1698, 1386, 1352, 1211, 744, 701 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.34–7.18 (m, 10H), 4.66–4.62 (m, 1H), 4.19–4.14 (m, 2H), 3.28 (dd, *J* = 13.5, 3.6 Hz, 1H), 3.03–2.93 (m, 2H), 2.77–2.71 (m, 3H), 2.04 (tt, *J* = 7.8, 7.8 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 173.0, 153.4, 141.5, 135.3, 129.4, 128.9, 128.5, 128.4, 127.3, 126.0, 66.2, 55.1, 37.9, 35.1, 35.0, 25.8; HRMS Calcd. for C₂₀H₂₁NNaO₃ [M+Na⁺] 346.1419, found 346.1418.

(S)-4-Isopropyl-3-(4-phenylbutanoyl)oxazolidin-2-one (14e)

According to the general procedure described for 10a, imide 14e (106 mg, 0.384 mmol, 99%) was obtained from 4phenylbutyric acid (9j) (64.0 mg, 0.389 mmol) and (S)-4isopropyl-2-oxazolidinone (13e) (125 mg, 0.968 mmol). The reaction using equimolar amount of 13e with Boc₂O (1.5 eq) gave imide 14e in 85% yield; a white solid; Mp 26-27 °C (hexanes-AcOEt); $[\alpha]_{D}^{28}$ +68.1 (c 1.00, CHCl₃); IR (neat) 2946, 1781, 1701, 1387, 1206, 701 cm⁻¹; ¹H NMR (600 MHz, $CDCl_3$) δ 7.30–7.18 (m, 5H), 4.41 (ddd, J = 9.0, 7.5, 2.4 Hz, 1H), 4.25 (dd, J = 9.0, 9.0 Hz, 1H), 4.19 (dd, J = 9.0, 2.4 Hz, 1H), 3.04-2.99 (m, 1H), 2.95-2.90 (m, 1H), 2.69 (t, J = 7.2Hz, 2H), 2.39–2.33 (m, 1H), 2.05–1.94 (m, 2H), 0.91 (d, J =6.6 Hz, 3H), 0.87 (d, J = 6.6 Hz, 3H); ¹³C NMR (150 MHz, CDCl₃) & 173.0, 154.0, 141.5, 128.5, 128.3, 125.9, 63.3, 58.4, 35.1, 35.0, 28.4, 26.0, 18.0, 14.6; HRMS Calcd. for $C_{16}H_{21}NNaO_3$ [M+Na⁺] 298.1419, found 298.1412.

N-Acetyl-N-4-diphenylbutanamide (14f)

According to the general procedure described for **10a**, imide **14f** (142 mg, 0.504 mmol, quant) was obtained from 4phenylbutyric acid (**9j**) (83.0 mg, 0.504 mmol) and acetanilide (**13f**) (170 mg, 1.26 mmol); a colorless oil; IR (neat) 2937, 1707, 1491, 1366, 1236, 1121, 697 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) & 7.46–7.39 (m, 3H), 7.27–7.24 (m, 2H), 7.19–7.09 (m, 5H), 2.61 (t, J = 7.2 Hz, 2H), 2.52 (t, J = 7.2 Hz, 2H), 2.31 (s, 3H), 1.94 (tt, J = 7.2, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) & 175.5, 173.0, 141.5, 139.1, 129.7, 128.8, 128.4, 128.3, 125.9, 37.7, 35.0, 27.0, 26.2 (One signal is missing due to overlap); HRMS Calcd. for C₁₈H₁₉NNaO₂ [M+Na⁺] 304.1313, found 304.1291.

N-(2-Bromophenyl)-N-formyl-4-phenylbutanamide (14g)

According to the general procedure described for 10a, imide 43 14g (137 mg, 0.397 mmol, 94%) was obtained from 4-44 phenylbutyric acid (9j) (69.0 mg, 0.420 mmol) and 2-45 (bromophenyl)formamide (13g) (210 mg, 1.05 mmol); a white 46 solid; Mp 61-62 °C (hexanes-AcOEt); IR (neat) 2978, 1728, 47 1704, 1474, 1305, 1201, 1161, 751, 701 cm⁻¹; ¹H NMR (600 48 MHz, CDCl₃) δ 9.56 (s, 1H), 7.72 (dd, J = 7.8, 1.2 Hz, 1H), 49 7.42 (dd, J = 7.8, 6.0 Hz, 1H), 7.33 (ddd, J = 8.4, 7.8, 1.2 Hz, 50 1H), 7.27–7.24 (m, 2H), 7.18 (dd, J = 7.8, 7.8 Hz, 2H), 7.11 51 (d, J = 7.8 Hz, 2H), 2.66-2.57 (m, 2H), 2.21-2.20 (m, 2H),2.00-1.94 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 174.4, 52 53 161.6, 141.0, 134.7, 133.9, 131.0, 130.6, 128.9, 128.41, 128.37, 126.1, 123.5, 34.9, 34.7, 25.3; HRMS Calcd. for 54 $C_{17}H_{16}BrNNaO_{2} [M^{+}+H] 368.0262$, found 368.0248. 55

N-Acetyl-N-(2-bromophenyl)-4-phenylbutanamide (14h) According to the general procedure described for 10a, imide 14h (142 mg, 0.396 mmol, 99%) was obtained from 4-phenylbutyric acid (9j) (66.0 mg, 0.400 mmol) and 2-bromoacetanilide (13h) (213 mg, 1.00 mmol); a white solid;

Mp 56-57 °C (hexanes-AcOEt); IR (neat) 2978, 1716, 1472, 1366, 1235, 1215, 1129, 756, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.69 (dd, J = 8.1, 1.2 Hz, 1H), 7.41 (ddd, J = 8.4, 7.8, 1.2 Hz, 1H), 7.31–7.25 (m, 3H), 7.20–7.14 (m, 4H), 2.63 (t, J = 7.2 Hz, 2H), 2.54 (t, J = 7.8 Hz, 2H), 2.32 (s, 3H), 1.96 (tt, J = 7.8, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 174.7, 172.2, 141.5, 138.5, 133.7, 130.7, 130.4, 128.8, 128.4, 128.3, 125.9, 123.9, 37.4, 35.0, 26.7, 26.0; HRMS Calcd. for C₁₈H₁₈BrNNaO₂ [M⁺+H] 382.0419, found 382.0408.

N-(2-Bromophenyl)-*N*-(4-phenylbutanoyl)benzamide (14i) According to the general procedure described for 10a, imide 14i (177 mg, 0.420 mmol, 95%) was obtained from 4phenylbutyric acid (9j) (72.0 mg, 0.440 mmol) and 2-(bromophenyl)benzamide (13i) (302 mg, 1.10 mmol); a colorless oil; IR (neat) 2954, 1714, 1693, 1472, 1298, 699 cm⁻¹; ¹H NMR (600 MHz, CDCl₃, a mixture of two rotamers) δ 7.66–7.62 (m, 2H), 7.44–7.14 (m, 12H), 2.75–2.62 (m, 4H), 2.08–2.02 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 175.8, 172.0, 141.5, 138.5, 135.2, 133.7, 131.8, 131.3, 130.0, 128.49, 128.46, 128.45, 128.36, 128.1, 125.9, 123.6, 37.1, 35.1, 26.4; HRMS Calcd. for C₂₃H₂₀BrNNaO₂ [M⁺+H] 444.0575, found 444.0567.

N-Acetyl-N-(2-methoxyphenyl)-4-phenylbutanamide (14j)

According to the general procedure described for **10a**, imide **14j** (97.4 mg, 0.313 mmol, 87%) was obtained from 4phenylbutyric acid (**9j**) (59.0 mg, 0.359 mmol) and 2acetanisidine (**13j**) (148 mg, 0.897 mmol); a pale yellow solid; Mp 36-37 °C (hexanes-AcOEt); IR (neat) 2954, 1711, 1499, 1367, 1280, 1248, 1224, 1023, 753 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.38 (dd, J = 7.5, 7.2 Hz, 1H), 7.25 (dd, J = 7.5, 7.2 Hz, 2H), 7.18–7.13 (m, 3H), 7.05 (d, J = 7.2 Hz, 1H), 7.01 (dd, J = 8.4, 7.5 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 3.78 (s, 3H), 2.61 (t, J = 7.2 Hz, 2H), 2.52 (br m, 2H), 2.30 (s, 3H), 1.93 (tt, J = 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 175.5, 173.0, 154.8, 141.7, 130.3, 130.0, 128.4, 128.3, 127.8, 125.8, 121.2, 111.9, 55.6, 37.0, 35.0, 26.5, 26.1; HRMS Calcd. for C₁₉H₂₁NNaO₃ [M+Na⁺] 334.1419, found 334.1424.

N-Acetyl-N-(3-methoxyphenyl)-4-phenylbutanamide (14k) According to the general procedure described for 10a, imide 14k (101 mg, 0.324 mmol, 94%) was obtained from 4phenylbutyric acid (9i) (57.0 mg, 0.346 mmol) and 3acetanisidine (13k) (143 mg, 0.866 mmol). The reaction using equimolar amount of 13k with Boc₂O (1.5 eq) gave imide 14k in 81% yield; a colorless oil; IR (neat) 2954, 1709, 1604, 1489, 1367, 1292, 1212, 1030, 698 cm⁻¹; ¹H NMR (600 MHz, $CDCl_3$) δ 7.34 (dd, J = 8.4, 8.1 Hz, 1H), 7.27–7.25 (m, 2H), 7.19–7.13 (m, 3H), 6.95–6.94 (m, 1H), 6.70–6.68 (m, 1H), 6.63-6.62 (m, 1H), 3.80 (s, 3H), 2.61 (t, J = 7.8 Hz, 2H), 2.55(t, J = 7.8 Hz, 2H), 2.33 (s, 3H), 1.94 (tt, J = 7.8, 7.8 Hz, 2H);¹³C NMR (150 MHz, CDCl₃) δ 175.5, 172.9, 160.6, 141.5, 140.1, 130.4, 128.4, 128.3, 125.9, 120.9, 114.6, 114.4, 55.4, 37.6, 35.0, 27.0, 26.2; HRMS Calcd. for C₁₉H₂₁NNaO₃ [M+Na⁺] 334.1419, found 334.1418.

N-Acetyl-*N*-(3-(methylthio)phenyl)-4-phenylbutanamide (14l)

According to the general procedure described for **10a**, imide **14l** (112 mg, 0.342 mmol, 94%) was obtained from 4phenylbutyric acid (**9j**) (60.0 mg, 0.365 mmol) and anilide **13l** (165 mg, 0.912 mmol). The reaction using equimolar amount

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of 13l with Boc₂O (1.5 equiv.) gave imide 14l in 85% yield; a colorless oil; IR (neat) 2954, 1710, 1587, 1366, 1235, 1217, 1125, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.35 (dd, J = 7.2, 7.2 Hz, 1H), 7.28–7.25 (m, 3H), 7.18 (dd, J = 7.2, 7.2 Hz, 1H), 7.13 (d, J = 6.6 Hz, 2H), 6.95 (dd, J = 2.4, 2.4 Hz, 1H), 6.85 (dd, J = 7.5, 2.4 Hz, 1H), 2.62 (t, J = 6.6 Hz, 2H), 2.52 (t, JJ = 7.8 Hz, 2H), 2.47 (s, 3H), 2.33 (s, 3H), 1.94 (tt, J = 7.8, 6.6Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 175.4, 172.9, 141.4, 140.8, 139.6, 129.9, 128.4, 128.3, 126.5, 126.3, 125.9, 125.2, 37.6, 34.9, 27.0, 26.2, 15.5; HRMS Calcd. for C₁₉H₂₁NNaO₂S [M+Na⁺] 350.1191, found 350.1193.

N-Acetyl-N-(4-methoxyphenyl)-4-phenylbutanamide (14m) According to the general procedure described for 10a, imide 14m (79.5 mg, 0.256 mmol, 98%) was obtained from 4phenylbutyric acid (9i) (43.0 mg, 0.260 mmol) and 4acetanisidine (13m) (108 mg, 0.654 mmol); a colorless oil; IR (neat) 2954, 1708, 1509, 1366, 1248, 1219, 1028 cm⁻¹; ¹H NMR (600 MHz, CDCl₂, a mixture of two rotamers) δ 7.27-7.25 (m, 2H), 7.19–7.13 (m, 3H), 7.01–6.98 (m, 2H), 6.95– 6.93 (m, 2H), 3.83 (s, 3H), 2.61 (t, J = 7.2 Hz, 2H), 2.52 (t, J = 7.8 Hz, 2H), 2.32 (s, 3H), 1.94 (tt, J = 7.8, 7.2 Hz, 2H); ^{13}C NMR (150 MHz, CDCl₃) δ 175.8, 173.3, 159.6, 141.5, 131.6, 129.7, 128.4, 128.3, 125.9, 114.9, 55.4, 37.7, 35.0, 27.0, 26.2; HRMS Calcd. for $C_{19}H_{21}NNaO_3$ [M+Na⁺] 334.1419, found 334.1434.

N-Acetyl-N-(2,6-dimethylphenyl)-4-phenylbutanamide (14n)

According to the general procedure described for 10a, imide 14n (122 mg, 0.395 mmol, 84%) was obtained from 4phenylbutyric acid (9i) (77.0 mg, 0.467 mmol) and 2,6dimethylacetanilide (13n) (191 mg, 1.17 mmol); a white solid; Mp 29-30 °C (hexanes-AcOEt); IR (neat) 2954, 1708, 1367, 1254, 1224, 773, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 7.27–7.12 (m, 8H), 2.62 (t, J = 7.2 Hz, 2H), 2.48 (t, J = 7.2Hz, 2H), 2.27 (s, 3H), 2.09 (s, 6H), 1.95 (tt, J = 7.2, 7.2 Hz, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 175.1, 172.6, 141.5, 137.2, 135.6, 128.9, 128.8, 128.4, 128.3, 125.9, 36.9, 35.0, 26.3, 26.1, 17.8; HRMS Calcd. for $C_{20}H_{23}NNaO_2$ [M+Na⁺] 332.1626, found 332.1656.

N-Acetyl-N-(naphthalen-1-yl)-4-phenylbutanamide (140)

42 According to the general procedure described for 10a, imide 43 140 (120 mg, 0.362 mmol, 92%) was obtained from 4-44 phenylbutyric acid (9j) (65.0 mg, 0.394 mmol) and 1-45 acetamidonaphthalene (130) (182 mg, 0.983 mmol). The 46 reaction using equimolar amount of 130 with Boc₂O (1.5 eq) 47 gave imide 140 in 91% yield; a colorless oil; IR (neat) 2954, 48 1709, 1366, 1219, 776 cm⁻¹; ¹H NMR (600 MHz, CDCl₃, a 49 mixture of two rotamers) & 7.93-7.91 (m, 2H), 7.65-7.63 (m, 50 1H), 7.55–7.50 (m, 3H), 7.29 (d, J = 7.2 Hz, 1H), 7.23 (dd, J =51 7.8, 7.2 Hz, 2H), 7.15 (dd, J = 7.8, 7.2 Hz, 1H), 7.08 (d, J =52 7.8 Hz, 2H), 2.67–2.53 (m, 3H), 2.49–2.44 (m, 1H), 2.34 (s, 3H), 1.96–1.90 (m, 2H); ¹³C NMR (150 MHz, CDCl₃) δ 175.8, 53 173.2, 141.5, 135.5, 134.5, 130.5, 129.5, 128.7, 128.4, 128.3, 54 127.7, 126.9, 126.7, 125.9, 125.6, 121.5, 37.3, 34.9, 26.7, 55 26.2; HRMS Calcd. for C₂₂H₂₁NNaO₂ [M+Na⁺] 354.1470, 56 found 354.1480. 57

4-Phenyl-N-pivaloyl-N-(pyridin-2-yl)butanamide (14p) 58

According	to the gen	eral proc	edure d	descril	bed for 10)a , im	ide
14p (71.3	mg, 0.220) mmol,	54%)	was	obtained	from	4-

phenylbutyric acid (9j) (67.0 mg, 0.407 mmol) and 2-(pivaloylamino)pyridine (13p) (182 mg, 1.02 mmol); a colorless oil; IR (neat) 2954, 1698, 1588, 1466, 1434, 1280, 1140, 747, 700 cm⁻¹; ¹H NMR (600 MHz, CDCl₃) δ 8.41 (d, J = 4.8 Hz, 1H), 7.76 (ddd, J = 8.7, 7.2, 1.2 Hz, 1H), 7.36 (d, J =7.2 Hz, 1H), 7.28–7.26 (m, 2H), 7.22–7.17 (m, 4H), 2.69 (t, J = 7.2 Hz, 2H), 2.51 (t, J = 7.2 Hz, 2H), 2.06 (tt, J = 7.2, 7.2 Hz, 2H), 1.10 (s, 9H); ¹³C NMR (150 MHz, CDCl₃) δ 186.5, 174.7, 152.0, 148.4, 141.5, 138.0, 128.5, 128.3, 125.9, 122.2, 121.8, 44.0, 35.7, 35.1, 28.4, 26.6; HRMS Calcd. for $C_{20}H_{24}N_2NaO_2$ [M+Na⁺] 347.1735, found 347.1726.

Procedure for Multi-Gram Scale Reaction

Caution! Because the reaction generates CO₂ gas, the multigram scale reaction should be conducted in flask equipped with balloon or under the open-air condition.

Methyl 4-(1H-indol-1-yl)-4-oxobutanoate (10a)

A 500 mL flask equipped with a magnetic stirring bar, was charged with Boc₂O (20.6 g, 94.6 mmol). A solution of monomethyl succinate (9a) (5.00 g, 37.8 mmol), indole (1) (11.0 g, 94.6 mmol), DMAP (231 mg, 1.89 mmol), and 2,6-lutidine (440 µL, 3.78 mmol) in MeCN (83 mL) were added to the flask at room temperature. Then, the reaction mixture was warmed to 28 °C by water bath. After stirring at 28 °C for 24 h under argon atmosphere, the resulting mixture was concentrated under reduced pressure to give a crude oil, which was purified by silica gel column chromatography (AcOEt/hexanes = 1:5) to give N-acyl indole 10a (8.46 g, 36.6 mmol, 97%).

N-Acetyl-*N*-(naphthalen-1-yl)-4-phenylbutanamide (140)

A 500 mL flask equipped with a magnetic stirring bar and argon balloon, was charged with Boc₂O (10.6 g, 48.6 mmol). A solution of 4-phenylbutyric acid (9i) (5.32 g, 32.4 mmol), 1acetamidonaphthalene (130) (6.00 g, 32.4 mmol), DMAP (200 mg, 1.64 mmol), and 2,6-lutidine (380 µL, 3.24 mmol) in MeCN (80 mL) were added to the flask at room temperature. Then, CH₂Cl₂ (100 mL) was added to a solution, and the reaction mixture was warmed to 28 °C by water bath. After stirring at 28 °C for 24 h under argon atmosphere, the resulting mixture was concentrated under reduced pressure to give a crude oil, which was purified by silica gel column chromatography (hexanes/AcOEt = 5:1) to give imide 140 (10.1 g, 30.5 mmol, 94%).

ASSOCIATED CONTENT

Supporting Information

Copies of ¹H and ¹³C-NMR spectra of compounds 10a-10w, 12a-12n, and 14a-14p. Copy of HPLC chromatogram of 10t. This materials is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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The authors declare no competing financial interest.

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