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Tandem Synthesis of Amides and Secondary Amines from Esters with Primary Amines under Solvent-Free Conditions

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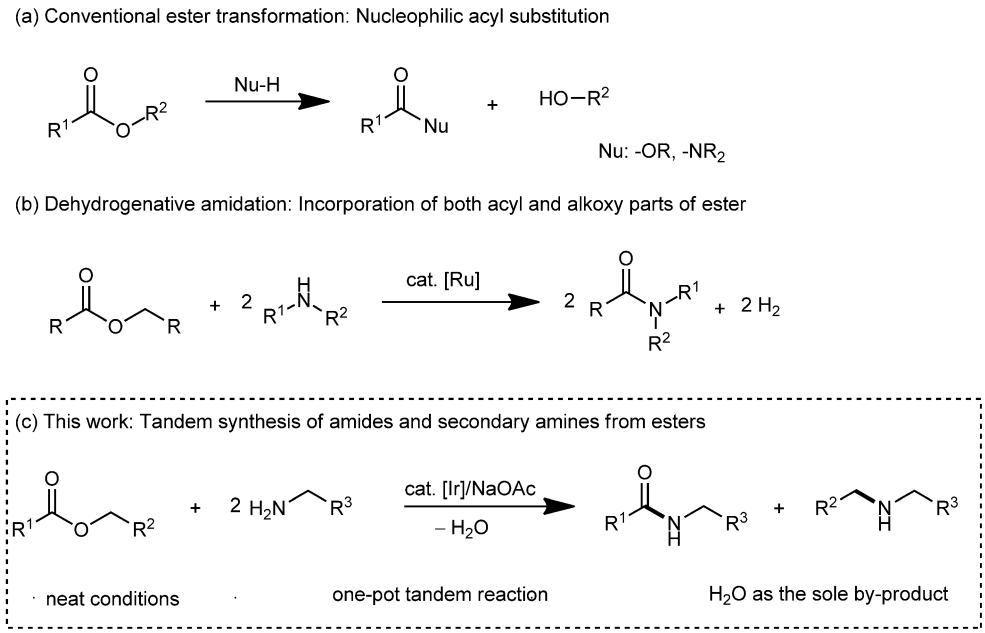
Abstract: An iridium(III)-catalyzed tandem synthesis of amides and amines from esters under solvent-free conditions is described. A commercially available iridium(III) complex, $[Cp^*IrCl_2]_2$, with sodium acetate showed the best activity for the synthesis of amides and secondary amines. The amide was formed by ester-amide exchange which generates an alcohol *in situ* which is subsequently transformed to a secondary amine *via* hydrogen autotransfer. This synthetic protocol with high atom economy generates water as the sole by-product and can afford amides and amines from various esters in a one-pot reaction, expanding the synthetic versatility of ester transformations.

Keywords: amides; amines; esters; hydrogen transfer; iridium

Introduction

Esters are one of the most common functional groups in nature and constitute an important class of carboxylic acid derivatives.[1] They are present in animal fats and are responsible for the pleasant aroma of vegetable oils. In biological systems, peptide bonds are formed by the enzymatic conversion of esters catalyzed by ribosomes. Many classical routes and catalytic transformations of esters, including ester hydrolysis,



Scheme 1. Different methods for ester transformation.

transesterification, and ester reduction to alcohol/aldehyde, are well documented.[1,2] In addition, the ester-amide exchange reaction is an important process and catalytic methods have also been reported.[3]

Recently, the Mashima group demonstrated that a catalytic amount of sodium methoxide is capable of converting various esters into amides under mild conditions.[3a] The development of catalytic protocols for such reactions has been oriented toward the efficient nucleophilic acyl substitutions of esters, with subsequent liberation of the corresponding alcohol (Scheme 1a). Methyl or ethyl esters have been commonly used thereby producing methanol or ethanol, respectively, as the corresponding alcohol.

One-pot multiple functionalization facilitates more than two transformations forming several bonds with less waste and greater economic benefits.[4] Although numerous synthetic transformations of esters have been reported, few attempts have been made to utilize the generated alcohols from esters in an one-pot reaction. Such a reaction would be attractive as the synthetic versatility of ester transformations could be enhanced. The seminal work by the Milstein group in the synthesis of amides from esters demonstrated that both the acyl and alkoxy parts of the ester starting material participated in the reaction by sequential ruthenium-catalyzed transformations (Scheme 1b).[3b]

The transition metal-catalyzed alkylation of amines with alcohols is one of the most promising methods for the synthesis of secondary amines.[5] The reaction proceeds by "borrowing hydrogen", also known as the hydrogen autotransfer method. The mechanism involves the dehydrogenation of the alcohol to the corresponding carbonyl compound followed by the formation of an imine and its reduction to an amine by the metal-hydride complex formed in the first step.

We focused on the fact that esters provide alcohols that can be used as an amine alkylation source. Hence we planned to develop a novel C–N bond formation method involving the following: (i) the formation of amide bonds by the nucleophilic acyl substitution of esters with amines and (ii) the synthesis of secondary amines by the reaction of the *in situ* generated alcohols with primary amines by the borrowing hydrogen method. To the best of our knowledge, this is the first report that documents the full utilization of esters as the direct carbon sources for amides and amines in a one-pot sequential reaction.

Results and Discussion

In order to realize our plan, the reaction of benzyl acetate (**1a**) with phenethylamine (**2a**) was chosen as the model reaction. Based on reported systems for the alkylation of amines with alcohols, we evaluated a series of iridium[6] and ruthenium[7] catalytic systems (Table 1). Initially the catalytic system consisting of $[Ru(p\text{-cymene})Cl_2]_2$, a phosphine ligand (dppf) and K_2CO_3[7c] afforded 64% of *N*-2-(phenylethyl)acetamide (**3a**) and only a trace amount of *N*-benzyl-2-phenethylamine (**4a**) (Table 1, entry 1). However, changing

Table 1. Optimization of reaction conditions.

Entry[a]	Catalyst (mol%)	Base (mol%)	Yield of **3a**[b]	Yield of **4a**[b]
1 (A)	$[Ru(p\text{-cymene})Cl_2]_2$ (2.5)/dppf[c] (5 mol%)	K_2CO_3 (10)	64%	4%
2 (B)	$[Ru(p\text{-cymene})Cl_2]_2$ (2.5)/dppf[c] (5 mol%)	K_2CO_3 (10)	50%	24%
3 (B)	$[Ru(benzene)Cl_2]_2$ (2.5)/dppf[c] (5 mol%)	K_2CO_3 (10)	60%	26%
4 (B)	$[(COD)IrCl]_2$ (2.5)	K_2CO_3 (10)	41%	9%
5 (B)	$Ir(CO)Cl(PPh_3)_2$ (2.5)	K_2CO_3 (10)	98%	16%
6 (B)	$IrH(CO)(PPh_3)_3$ (2.5)	K_2CO_3 (10)	63%	27%
7 (B)	$[Cp^*IrCl_2]_2$ (2.5)	K_2CO_3 (10)	60%	31%
8 (A)	$[Cp^*IrCl_2]_2$ (2.5)	K_2CO_3 (10)	80%	44%
9 (A)	$[Cp^*IrCl_2]_2$ (2.5)	K_2CO_3 (5)	81%	38%
10 (A)	$[Cp^*IrCl_2]_2$ (2.5)	Na_2CO_3 (5)	62%	46%
11 (A)	$[Cp^*IrCl_2]_2$ (2.5)	$NaHCO_3$ (5)	69%	57%
12 (A)	$[Cp^*IrCl_2]_2$ (2.5)	Cs_2CO_3 (5)	63%	52%
13 (A)	$[Cp^*IrCl_2]_2$ (2.5)	NaOMe (5)	90%	73%
14 (A)	$[Cp^*IrCl_2]_2$ (2.5)	NaOMe (2)	73%	48%
15 (A)	$[Cp^*IrCl_2]_2$ (2.5)	NaOAc (5)	93%	66%
16 (A)	$[Cp^*IrCl_2]_2$ (2.5)	NaOAc (2.5)	99%	71%
17 (C)	$[Cp^*IrCl_2]_2$ (1.25)	NaOAc (2.5)	>99%	73%
18 (D)	**$[Cp^*IrCl_2]_2$ (1.25)**	**NaOAc (2.5)**	**>99%**	**77%**

[a] *Reaction conditions:* (A) solvent, toluene (0.8 M); reaction temperature, 115 °C; reaction time, 36 h; (B) solvent, xylene (0.8 M); reaction temperature, 145 °C; reaction time, 36 h; (C) neat; reaction temperature, 115 °C; reaction time, 36 h; (D) neat; reaction temperature, 115 °C; reaction time, 24 h.
[b] GC yields using dodecane as the internal standard.
[c] dppf = 1,1′-bis(diphenylphosphino)ferrocene.

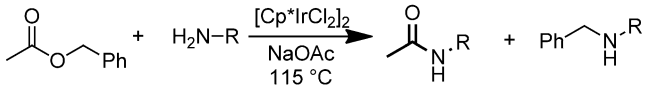
the catalyst system to $[Cp^*IrCl_2]_2$ and K_2CO_3[6e] resulted in improved yields (Table 1, entry 7). Therefore, we investigated several other bases in combination with $[Cp^*IrCl_2]_2$ at different catalyst loadings (Table 1, entries 7–18). Compared to the carbonate bases, NaOMe showed better activity in toluene under reflux for 36 h. However, on reducing the base loading, the yields decreased, particularly that for **4a** (Table 1, entries 13 and 14). Gratifyingly, the use of 2.5 mol% of NaOAc in toluene under reflux for 36 h afforded **3a** and **4a** in excellent and good yields, respectively (Table 1, entry 16). The reduction of the catalyst loading to 1.25 mol% did not affect the yields of products (Table 1, entry 17). To our delight, the reaction run without a solvent resulted in the highest yield at a reduced reaction time of 24 h (Table 1, entry 18).[8]

With the optimized reaction conditions in hand (Table 1, conditions D), amides and secondary amines were synthesized from diverse esters and primary amines. First, the reactions of **1a** and various primary amines were explored (Table 2); the corresponding amides and secondary amines were obtained in good to high yields. In general, the yields of amide were higher than those of amines. Benzylamines afforded both amides and secondary amines (Table 2, entries 2, 9–11). Cyclohexylamine (**2e**) and cyclopentylamine (**2f**) also smoothly afforded the corresponding amides and amines (Table 2, entries 5 and 6). In contrast, the less basic aniline was not reactive for the synthesis of both amides and amines as reported in other cases (Table 2, entry 12).[3a,6d]

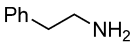
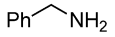
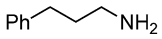
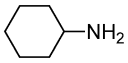
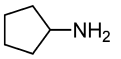
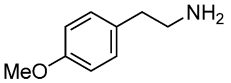
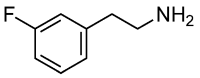
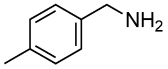
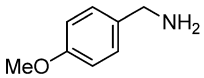
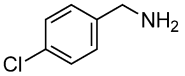
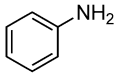
Next, the reactions of **2a** with different esters were investigated. Benzyl acetates with electron-withdrawing and electron-donating substituents showed similar results in the synthesis of the corresponding amides (Table 3, entries 1 and 2). However, benzyl acetate with an electron-donating substituent resulted in slightly lower yields of secondary amine (Table 3, entry 2). Benzyl benzoate (**1d**) was less successful in this reaction than the acetate esters probably because of the steric hindrance (Table 3, entry 3). However, the length of the alkyl chains on the acyl part of esters did not adversely affect the reaction (Table 3, entries 4 and 7). The substituents on 1-methylbenzyl acetate (**1f**) and piperonyl acetate (**1g**) interrupted the corresponding amine formation (Table 3, entries 5 and 6). *n*-Hexyl acetate (**1i**) also afforded **3a** and *N*-hexyl-2-phenylethylamine (**6i**) (Table 3, entry 8).

Avoidance of organic solvent is an important issue in modern organic synthesis in order to reduce the environmental impact.[9] It is of much benefit for large-scale synthesis. Gratifyingly, our developed conditions could be readily scaled up to gram quantities to obtain **3a** and **4a** from **1a** (Table 4).[10] It is notable that the reduced catalyst loading showed similar catalytic activity while the reaction with 0.3 mol% of catalyst retarded both the formation of amide and amine.

Table 2. Synthesis of amides and secondary amines from different amines and **1a**.



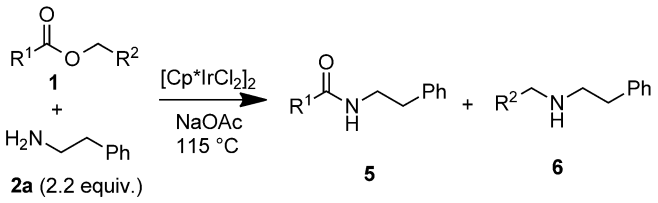
1a **2** (2.2 equiv.) **3** **4**

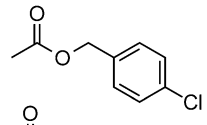
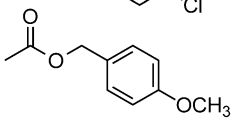
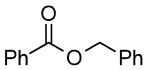
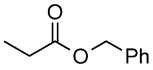
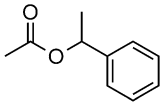
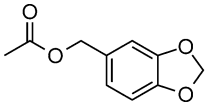
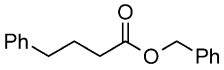
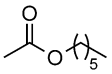
Entry	Amines		Yield [%][b] of 3	Yield [%][b] of 4
1		**2a**	**3a:** 99	**4a:** 69
2		**2b**	**3b:** 98	**4b:** 67
3		**2c**	**3c:** 99	**4c:** 66
4		**2d**	**3d:** 86	**4d:** 65
5		**2e**	**3e:** 82	**4e:** 60
6		**2f**	**3f:** 98	**4f:** 40
7		**2g**	**3g:** 86	**4g:** 75
8		**2h**	**3h:** 99	**4h:** 66
9		**2i**	**3i:** 90	**4i:** 70
10		**2j**	**3j:** 90	**4j:** 47
11		**2k**	**3k:** 90	**4k:** 67
12		**2l**	**3l:** 29	**4l:** 6

[a] *Reaction conditions:* **1a** (0.5 mmol, 1.0 equiv.), **2** (2.2 equiv.), $[Cp^*IrCl_2]_2$ (1.25 mol%), NaOAc (2.5 mol%), 24 h.
[b] Isolated yields.

Next, to gain mechanistic insights into the reaction, a kinetic study was performed by monitoring the progress of the reaction of **1a** with **2a** (Figure 1). At the initial stage of the reaction, the rate of the amide formation was very rapid. Benzyl alcohol was detected by gas chromatography (GC) analysis, indicating that the free alcohol was generated from the ester before forming the secondary amine. At approximately $T = 150$ min, the rate of **4a** formation surpassed

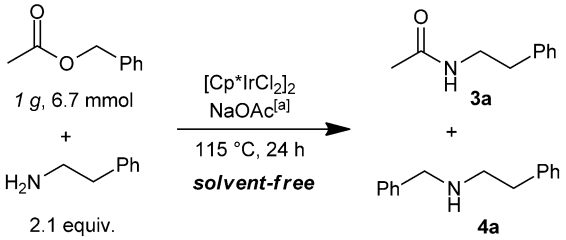
Table 3. Synthesis of amides and secondary amines from different esters and **2a**.



Entry	Esters		Yield [%][b] of 5	Yield [%][b] of 6
1		**1b**	**3a:** 98	**6b:** 69
2		**1c**	**3a:** 97	**6c:** 59
3		**1d**	**5d:** 68	**4a:** 62
4		**1e**	**5e:** 98	**4a:** 67
5		**1f**	**3a:** 82	**6f:** 30
6		**1g**	**3a:** 97	**6g:** 6
7		**1h**	**5h:** 73	**4a:** 69
8		**1i**	**3a:** 83	**6i:** 61

[a] *Reaction conditions:* **1** (0.5 mmol, 1.0 equiv.), **2a** (2.2 equiv.), $[Cp^*IrCl_2]_2$ (1.25 mol%), NaOAc (2.5 mol%), 24 h.
[b] Isolated yields.

Table 4. Gram-scale reaction.



$[Cp^*IrCl_2]_2$ [mol%]	**3a** [%][b]	**4a** [%][b]
1.25	98	71
0.6	92	65
0.5	94	64
0.3	77[c]	17[c]

[a] Equivalents same as that of the iridium catalyst.
[b] Isolated yields.
[c] GC yield with dodecane as the internal standard.

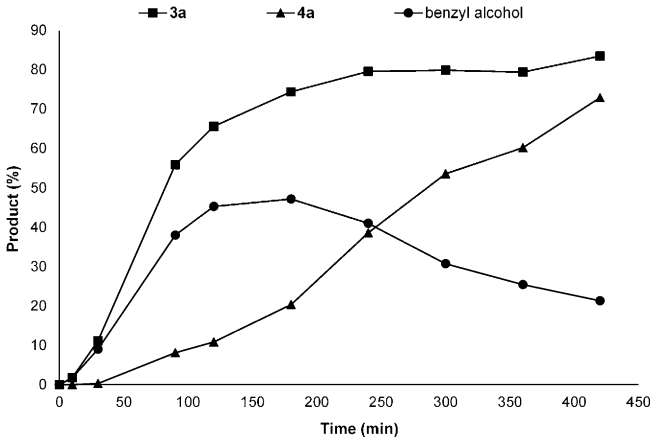


Figure 1. Reaction profile that shows the amount of product formed. *Reaction conditions:* **1a** (0.25 mmol, 1.0 equiv.), **2a** (2.2 equiv.), $[Cp^*IrCl_2]_2$ (1.25 mol%), NaOAc (2.5 mol%), 115 °C. The progress in the reaction was monitored by GC analysis using dodecane as the internal standard.

that of the alcohol formation thereby decreasing the alcohol concentration. We also conducted comparable experiments to probe the reaction profile in absence of iridium and base. As expected, the secondary amine was not detected in the reaction without the iridium complex. Furthermore, it also turned out that amide formation was accelerated by the iridium catalyst from the initial time of the reaction (Figure 2).

Based on the conducted experiments and previous reports,[6,8,11] a probable mechanism for the $[Cp^*IrCl_2]_2$-catalyzed synthesis of amides and secondary amines from esters is suggested (Scheme 2). First, the amide is formed by nucleophilic acyl substitution of the ester with primary amine. Next, the *in situ* generated alcohol is dehydrogenated and reacts with additional primary amine to form imine. Finally, hydrogenation of imine by hydrogen transfer from the iridium hydride affords the secondary amine.

Conclusions

In conclusion, an environmentally-friendly, atom-economic method was developed for synthesizing amides and secondary amines in one-pot using a simple iridium(III) catalytic system under solvent-free conditions, generating water as the sole by-product. Various amides and secondary amines were synthesized effi-

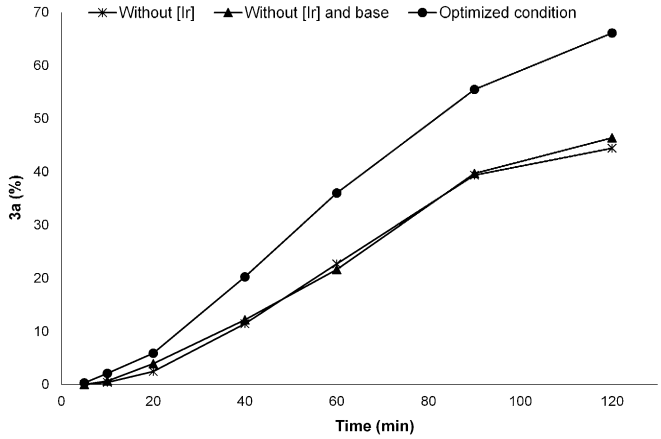


Figure 2. Reaction profile that shows the amount of amide **3a** formed. *Reaction conditions:* **1a** (0.25 mmol, 1.0 equiv.), **2a** (2.0 equiv.), 115 °C. The progress in the reaction was monitored by GC analysis using dodecane as the internal standard.

ciently from their corresponding primary amines and esters, even in gram-scale reactions. Notably, the current method utilizes esters as the direct carbon source for both amides and secondary amines.

Experimental Section

General Considerations

Unless otherwise noted, all reactions were carried out using a 4-mL vial in an argon-filled glove box. NMR spectra were recorded in $CDCl_3$ and residue solvent signals were used as a reference. Chemical shifts were reported in ppm and coupling constants in Hz. Multiplicity is indicated by one or more of the following: s (singlet); d (doublet); t (triplet): q (quartet); spt (septet); m (multiplet). All reagents and solvents, unless otherwise noted, were purchased from commercial suppliers and used as received without further purification. Esters **1b–1i** were either purchased or synthesized according to the literature.

GC Analysis of the Reaction Profile

Inside an argon-filled glove box, $[Cp^*IrCl_2]_2$ (2.5 mg, 1.25 mol%) and NaOAc (0.5 mg, 2.5 mol%) were added to an oven-dried 4-mL vial equipped with septum screw cap. Then **1a** (36 μL, 0.25 mmol), **2a** (69 μL, 0.55 mmol) were added into the vial using micro-syringes after the vial had been taken out of the glove box. The vials were individually prepared for 0 min, 5 min, 10 min, 20 min, 40 min, 60 min, 90 min, 120 min and heated at 115 °C. After the required time, the vial was removed from heating, quickly cooled down to a low temperature, the mixture diluted with dichloromethane and dodecane (22.7 μL, 0.1 mmol) as an internal standard was added to the vial. The sample was filtered with celite before analysis by GC.

General Procedure for the Synthesis of Amides and Secondary Amines with Different Primary Amines (Table 2)

$[Cp^*IrCl_2]_2$ (50 mg, 0.062 mmol), NaOAc (8.0 mg, 0.010 mmol) were added in an oven-dried vial inside the glove box. The vial was taken out and the ester (0.50 mmol) and amine (1.15 mmol) were added under an argon atmosphere. The mixture was heated to 115 °C for 24 h before being cooled to room temperature. Purification of the crude product was performed by flash column chromatography. All products were identified by spectral comparison with literature data.

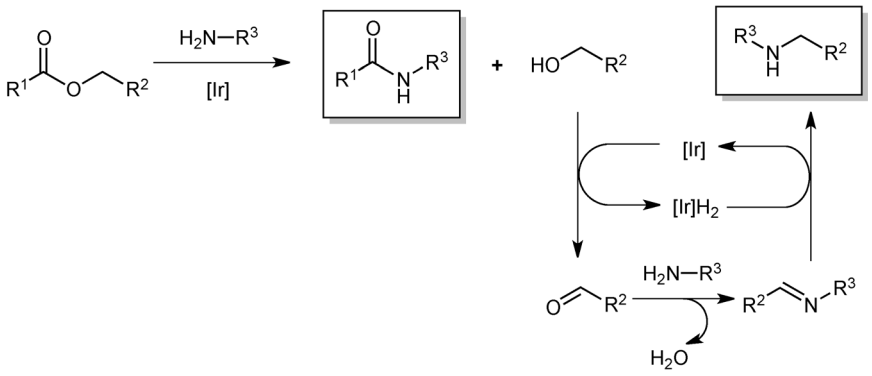
***N*-2-(Phenylethyl)acetamide (3a):**[12] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.20 (m, 5H), 5.52 (bs, 1H), 3.53 (dd, J = 12.9, 6.9 Hz, 2H), 2.83 (t, J = 6.9 Hz, 2H), 1.95 (s, 3H).

***N*-Benzyl-2-phenethylamine (4a):**[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.15 (m, 10H), 3.78 (s, 2H), 2.90–2.86 (m, 2H), 2.83–2.78 (m, 2H), 1.53 (s, 1H).

***N*-Benzylacetamide (3b):**[12] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 5H), 6.09 (bs, 1H), 4.38 (d, J = 5.7 Hz, 2H), 1.98 (s, 3H), 1.24 (s, 1H).

***N*-Benzyl-1-phenylmethanamine (4b):**[13] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.16 (m, 10H), 3.73 (s, 4H), 1.65 (s, 1H).

***N*-(3-Phenylpropyl)acetamide (3c):**[12] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.31 (m, 2H), 7.30–7.20 (m, 3H), 5.82 (bs, 1H), 3.41–3.27 (m, 2H), 2.78–2.62 (m, 2H), 2.00 (s, 3H), 1.91 (dt, J = 14.6, 7.5 Hz, 2H).



Scheme 2. Proposed mechanism.

***N*-Benzyl-3-phenylpropan-1-amine (4c):**[14] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.10 (m, 10H), 3.73 (s, 2H), 2.64–2.59 (m, 4H), 1.82–1.78 (m, 2H), 1.50 (s, 1H).

***N*-Heptylacetamide (3d):**[15] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.74 (bs, 1H), 3.26–3.12 (m, 2H), 1.94 (s, 3H), 1.50–1.40 (m, 2H), 1.30–1.21 (m, 8H), 0.85 (t, *J* = 6.7 Hz, 3H).

***N*-Benzylheptan-1-amine (4d):**[16] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.27–7.19 (m, 5H), 3.73 (s, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 1.55 (s, 1H), 1.48–1.43 (m, 2H), 1.25–1.23 (m, 8H), 0.82 (t, *J* = 6.5 Hz, 3H).

***N*-Cyclohexylacetamide (3e):**[17] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.57 (bs, 1H), 3.74–3.68 (m, 1H), 1.94 (s, 3H), 1.92–1.86 (m, 2H), 1.75–1.49 (m, 3H), 1.42–1.21 (m, 2H), 1.20–0.97 (m, 3H).

***N*-Benzylcyclohexanamine (4e):**[18] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.11 (m, 5H), 3.76 (s, 2H), 2.52–2.37 (m, 1H), 1.87 (d, *J* = 11.3 Hz, 2H), 1.74–1.62 (m, 2H), 1.60–1.43 (m, 2H), 1.29–0.99 (m, 5H).

***N*-Cyclopentylamide (3f):**[17] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.80 (bs, 1H), 4.22–4.10 (m, 1H), 1.99–1.93 (m, 2H), 1.91 (s, 3H), 1.68–1.59 (m, 2H), 1.59–1.49 (m, 2H), 1.34 (td, *J* = 12.8, 6.5 Hz, 2H).

***N*-Benzylcyclopentanamine (4f):**[19] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.26–7.16 (m, 5H), 3.71 (s, 2H), 3.05 (p, *J* = 6.7 Hz, 1H), 1.83–1.75 (m, 2H), 1.68–1.59 (m, 2H), 1.51–1.42 (m, 2H), 1.32 (td, *J* = 14.0, 7.8 Hz, 2H), 0.39 (s, 1H).

***N*-(4-Methoxyphenethyl)acetamide (3g):**[20] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.10 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.54 (bs, 1H), 3.78 (s, 3H), 3.50–3.42 (m, 2H), 2.74 (t, *J* = 7.0 Hz, 2H), 1.93 (s, 3H).

***N*-(4-Methoxyphenethyl)benzylamine (4g):**[21] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.15 (m, 5H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3.77 (s, 2H), 3.75 (s, 3H), 2.89–2.80 (m, 2H), 2.79–2.69 (m, 2H), 1.52 (s, 1H).

***N*-(3-Fluorophenethyl)acetamide (3h):**[22] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.25 (m, 2H), 6.98–6.88 (m, 3H), 5.44 (bs, 1H), 3.53–3.49 (m, 2H), 2.82 (t, *J* = 7.0 Hz, 2H), 1.95 (s, 3H).

***N*-(3-Fluorophenethyl)benzylamine (4h):** ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.30–7.21 (m, 6H), 6.99 (d, *J* = 7.3 Hz, 1H), 6.97–6.87 (m, 2H), 3.81 (s, 2H), 2.93 (t, *J* = 6.8 Hz, 1H), 2.84 (t, *J* = 6.8 Hz, 2H), 1.47 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 162.9 (d, *J* = 245.1 Hz), 142.5 (d, *J* = 7.23 Hz), 140.0, 129.8 (d, *J* = 8.6 Hz), 128.4, 128.0, 126.9, 124.3 (d, *J* = 2.9 Hz), 115.5 (d, *J* = 20.98 Hz), 113.0 (d, *J* = 20.98 Hz), 53.8, 50.1, 36.0; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −113.58; HR-MS (FAB): *m*/*z* = 230.1345, calcd. for $C_{15}H_{17}FN$ $[M+H]^+$: 230.1347.

***N*-(4-Methylbenzyl)acetamide (3i):**[12] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.19–7.13 (m, 4H), 5.85 (bs, 1H), 4.38 (d, *J* = 5.6 Hz, 2H), 2.34 (s, 3H), 2.01 (s, 3H).

***N*-(4-Methylbenzyl)benzylamine (4i):**[23] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.18 (m, 9H), 3.89–3.81 (m, 4H), 2.39 (s, 3H), 1.76 (s, 1H).

***N*-(4-Methoxybenzyl)acetamide (3j):**[12] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.19 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 5.97 (bs, 1H), 4.33 (d, *J* = 5.6 Hz, 2H), 3.79 (s, 3H), 1.98 (s, 3H).

***N*-(4-Methoxybenzyl)benzylamine (4j):**[19] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28–7.22 (m, 4H), 6.81–6.78 (m, 3H), 6.79 (d, *J* = 8.7 Hz, 2H), 3.72 (s, 5H), 3.67 (s, 2H), 1.76 (s, 1H).

***N*-(4-Chlorobenzyl)acetamide (3k):**[12] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.28 (d, *J* = 6.8 Hz, 2H), 7.19 (d, *J* = 7.9 Hz, 2H), 5.89 (bs, 1H), 4.37 (d, *J* = 5.1 Hz, 2H), 2.01 (s, *J* = 3.8 Hz, 3H).

***N*-(4-Chlorobenzyl)benzylamine (4k):**[24] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.19 (m, 9H), 3.76–3.71 (m, 4H), 1.61 (s, 1H).

***N*-Phenylacetamide (3l):**[25] ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 2H), 7.07–7.16 (m, 1H), 2.19 (s, 3H).

***N*-Benzylaniline (4l):**[6b] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.34–7.41 (m, 4H), 7.27–7.32 (m, 1H), 7.18–7.23 (m, 2H), 6.74–6.79 (m, 1H), 6.68 (dd, *J* = 8.8, 1.0 Hz, 2H), 4.35 (s, 2H).

General Procedure for the Synthesis of Amides and Secondary Amines with Different Esters (Table 3)

***N*-(4-Chlorobenzyl)phenethylamine (6b):**[26] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.19 (m, 9H), 3.77 (s, 2H), 2.91–2.79 (m, 4H), 1.52 (s, 1H).

***N*-(4-Methoxybenzyl)phenethylamine (6c):**[26] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.10 (m, 5H), 7.09 (d, *J* = 8.5 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 3.77 (s, 2H), 3.75 (s, 3H), 2.87–2.82 (m, 2H), 2.77–2.72 (m, 2H), 1.52 (s, 1H).

***N*-Phenethylbenzamide (5d):**[12] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70 (d, 2H), 7.47–7.22 (m, 8H), 6.33 (bs, 1H), 3.74–3.67 (m, 2H), 2.93 (t, *J* = 7.0 Hz, 2H).

***N*-Phenethylpropionamide (5e):**[27] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.10 (m, 5H), 5.50 (bs, 1H), 3.44 (m, 2H), 2.74 (t, *J* = 7.0 Hz, 2H), 2.08 (q, *J* = 7.6 Hz, 2H), 1.04 (t, *J* = 7.6 Hz, 3H).

***N*-(1-Methylbenzyl)phenethylamine (6f):**[7a] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.13 (m, 10H), 3.78 (q, *J* = 6.6 Hz, 1H), 2.81–2.68 (m, 4H), 1.33 (d, *J* = 6.6 Hz, 3H).

***N*-(2-Phenylethyl)-1,3-benzodioxole-5-methanamine (6g):** ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.17 (m, 5H), 6.79 (s, 1H), 6.71–6.73 (m, 2H), 5.91 (s, 2H), 3.70 (s, 2H), 2.92–2.85 (m, 2H), 2.84–2.77 (m, 2H), 1.52 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.6, 146.4, 140.0, 134.2, 128.7, 128.4, 126.1, 121.1, 108.6, 108.0, 100.8, 53.6, 50.3, 36.3; HR-MS (FAB): *m*/*z* = 256.1338, calcd. for $C_{16}H_{18}NO_2$ $[M+H]^+$: 256.1339.

***N*-Phenethyl-4-phenylbutanamide (5h):**[28] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.14 (m, 10H), 5.53 (bs, 1H), 3.56–3.50 (m, 2H), 2.80 (t, *J* = 7.0 Hz, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.11 (t, *J* = 7.6 Hz, 2H), 2.01–1.86 (m, 2H).

***N*-Hexyl-2-phenylethylamine (6i):**[29] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.24 (m, 5H), 3.34–3.28 (m, 2H), 3.25–3.11 (m, 2H), 3.04–2.90 (m, 2H), 2.02–1.87 (m, 2H), 1.64 (bs, 1H), 1.43–1.33 (m, 2H), 1.33–1.24 (m, 4H), 0.84 (t, *J* = 6.6 Hz, 3H), 1.63 (s, 1H).

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