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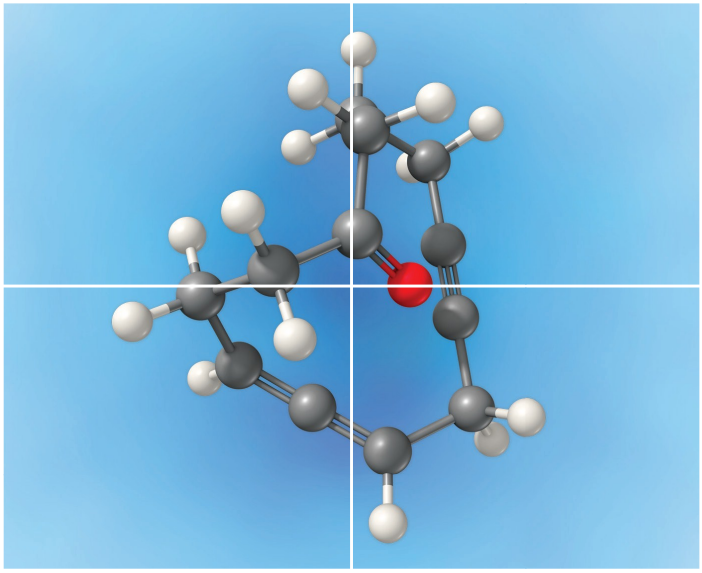

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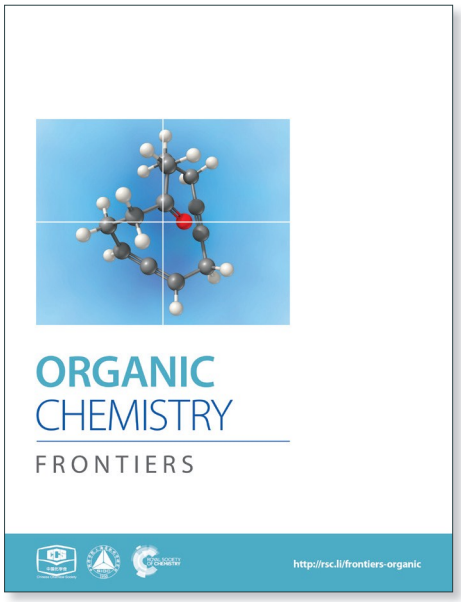

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ARTICLE TYPE

Simple, Versatile, and Chemoselective Reduction of Secondary Amides and Lactams to Amines with Tf_2O - $NaBH_4$ or Cp_2ZrHCl - $NaBH_4$ System

Pei-Qiang Huang*[a,b] and Hui Geng[a]

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The reduction of secondary amides to amines is an important transformation for the total synthesis of alkaloids and pharmaceuticals. General and chemoselective direct methods for this transformation are scarce. We report in this paper a simple method for the direct reduction of secondary amides, which uses only two reagents, triflic anhydride for amide activation, and $NaBH_4$ for reduction. Running under mild conditions (0 °C to r.t.), the reaction works well with several types of secondary amides including aromatic amides, aliphatic amides, and α,β-unsaturated amide. The reaction displays a good functional group tolerance for a series of reducible functional groups. The method is applicable to the direct reduction of C-H lithiation – functionalization products, and C-H activation – functionalization products. Moreover, chemoselective reduction of secondary lactams has been achieved using Cp_2ZrHCl - $NaBH_4$ combination.

Introduction

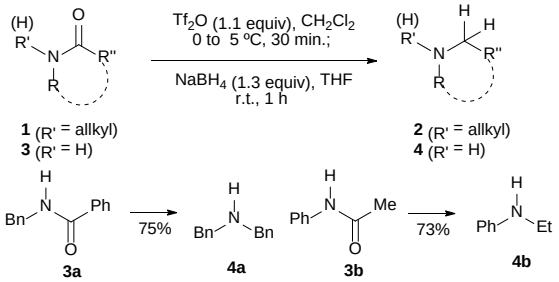
The reduction of amides to amines is an important transformation for the synthesis of bioactive alkaloids and *N*-containing medicinal agents.[1] Due to the high stability of amides, use of strong reducing agents[2] such as $LiAlH_4$,[3] diborane,[4] borane-THF/ SMe_2 complex,[5] and DIBAL-H[6] is generally required. In addition, sometimes the reduction reaction needs to be run under harsh conditions. As for the reduction of secondary amides, the classical Brown reduction with borane-THF/ SMe_2 complex is incompatible with alkenyl and alkynyl groups, and requires extra step to dissociate borane-amine adducts.[7] It is not a surprise that the classical methods are low functional group tolerant and may lead to undesired products.[3,8] These can account for the fact that stepwise protocols involving the pre-transformation of amides to thioamides[1e-i,l] or pre-transformation of secondary amides to imides[9] are methods of choice in the synthesis of alkaloids and medicinal agents.[1] To suit the needs of modern organic synthesis and pharmaceutical chemistry, development of chemoselective methods for the direct reduction of amides has attracted considerable attention, and significant progresses have been made in recent years.[10,11] However, chemoselective reduction of amides under mild conditions remains a challenging issue,[10a,b,e] in particular for secondary amides,[12] which contain both a highly stabilized carbonyl and an active proton. Only limited examples involving chemoselective reduction of secondary amides have been reported.[12]

General and chemoselective methods with a broad functional group tolerance are rare, which include Charette's chemoselective reduction utilizing Tf_2O/ 2-F-Py/ Et_3SiH/ Hantzsch ester hydride (HEH) system,[12b] Nagashima's Ru[11e] and Pt[10l] catalyzed hydrosilylations, Beller's zinc-catalyzed chemoselective reduction,[12c] and boronic acid catalyzed selective hydrosilylation,[12i] Reeves' Ru-catalyzed hydrosilylation,[12f] as well as Lou's low-valent titanium reduction.[12g] Moreover, secondary amides serve as powerful directing groups for both directed lithiation – functionalization[13] and C-H activation – functionalization.[14] Thus, simple methods for direct and chemoselective reduction of secondary amides are still highly demanding.[15]

As a continuation of our program on the development of synthetic methodology for the direct transformations of amides,[16] we disclosed recently the first general method for the direct reductive alkylation of secondary amides[15n] and a Tf_2O-based[17] method for the reduction of amides **1**/ **3** to give amines **2**/ **4** (Scheme 1).[10n] The latter report also includes secondary amides **3a** and **3b**. Herein, we report the results of a systematic investigation on the direct and chemoselective reduction of secondary amides to amines.

[a] *Department of Chemistry and Fujian Provincial Key Laboratory of Chemical Biology, Collaborative Innovation Centre of Chemistry for Energy Materials, College of Chemistry and Chemical Engineering, Xiamen University, Xiamen, Fujian 361005, PR China*
[b] *State Key Laboratory of Applied Organic Chemistry Lanzhou University, Lanzhou 730000, China*
E-mail: pqhuang@xmu.edu.cn

† Electronic Supplementary Information (ESI) available: ^1H and ^{13}C NMR spectra of all reduction products. This material is available free of charge via xxx. See DOI: 10.1039/b000000x/

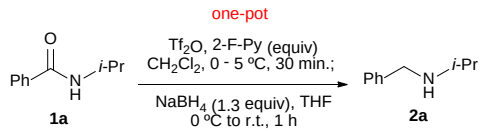


Scheme 1

Results and discussion

In our previous report,[10n] the optimal conditions defined for the direct reduction of tertiary amides were adapted for the reduction of secondary amides **3a** and **3b**. Thus in the present investigation, Tf_2O and $NaBH_4$ were keeped for the *in situ* amides activation and the reduction of the presumed imidoyl triflate intermediates, while other reaction parameters including solvent (THF, Et_2O, MTBE), equivalents of sodium borohydride (1.3-2.0 mol equiv) were re-examined. With Tf_2O/ CH_2Cl_2 - $NaBH_4$ (1.3 mol equiv)/ THF combination, the reduction of *N*-*i*-propylbenzamide **1a** gave amine **2a** in 74% yield along with 9% of the recovered starting amide (Table 1, entry 1). Next, the effects of 2-fluoropyridine (2-F-Py) was examined. As can be seen from Table 1, use of 0.5 mol equiv of 2-F-Py (Table 1, entry 2) resulted in an increase of yield of amine **2a** by 5%. However, the yield based on the recovered starting material remained the same. Surprisingly, use of more equiv of 2-F-Py led to a drop of yield (Table 1, entries 2-5), which is attributed to the competing reduction reaction of the 2-fluoropyridinium ion at a higher concentration. On balance of yield and atom economy, the optimal conditions for the amide reduction was defined as: Tf_2O (1.1 mol equiv)/ CH_2Cl_2 (0.25 M) - $NaBH_4$ (1.3 mol equiv)/ THF.

Table 1 The Effects of 2-Fluoropyridine on the Tf_2O-Activated Reduction of Secondary Amides

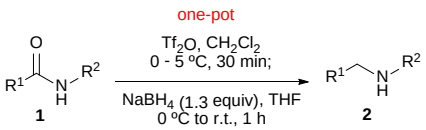


Entry	2-F-Py (equiv)	% yield of **2a**[a]
1	**0**	**74 (83)**[b]
2	**0.5**	**79 (83)**[b]
3	1.2	67 (*ca.* 67)[c]
4	1.5	66 (*ca.* 66)[c]
5	2.0	60 (*ca.* 60)[c]

[a] Isolated yield; [b] Yield based on the recovered starting amide; [c] only trace of the starting amide was observed on TLC.

With the optimal conditions in hand, the scope of the reduction was investigated, and the results are summarized in Table 2. We first examined the effects of substituents on the reduction of aromatic amides. As can be seen from entries 1 to 4 and entries 5 to 9 of Table 2, the reactions worked similarly for benzamide derivatives bearing both electron-donating groups (entries 2, 3 and 6) and electron-withdrawing groups (entries 4, 7-9) at *para*-position. Slightly lower yields were obtained from substrates bearing an electron donating group. *N*-*i*-Propyl and *N*-*c*-hexylbenzamides gave similar results (entries 1, 2 versus 5, 6). In addition to ether (entry 3), halo (entries 4, 7 and 8), and CF_3 (entry 9) groups, the functional group tolerance of the reaction was further examined. The results shown in entries 10-12 indicate that the reaction also tolerate *para*-substituted ester, cyano and nitro groups. α,β-Unsaturated amide **1m** also reacted chemoselectively to produce the corresponding amine **2m** in 65% yield (entry 13). Surprisingly, the reaction of *m*-bromobenzamide **1n** gave the corresponding amine **2n** in a lower yield of 64% (entry 14). Good yield was obtained with *N*-isopropyl-1-naphthamide (entry 15, yield: 78%). It is worthy of noting that *N*-isopropyl-3-phenylpropanamide **1p**, an aliphatic amide, also reacted smoothly to give amine **2p** in 70% yield (entry 16). However, the reduction of more hindered *N*-isopropyl-2-phenylbutanamide **1q** afforded the corresponding amine **2q** in a modest yield of 63% (entry 17). Interestingly, the reduction of (*S*)-*N*-(1-phenylethyl)benzamide **1r** produced the corresponding amine **2r** in 65% yield (entry 18).

Table 2 Tf_2O-Activated Reduction of Secondary Amides with $NaBH_4$



Entry	Substrate (R^1, R^2)	Product: % yield[a]
1	**1a** (Ph, *i*-Pr)	**2a:** 74 (83)[b]
2	**1b** (*p*-MeC_6H_4, *i*-Pr)	**2b:** 67 (74)[b]
3	**1c** (*p*-$MeOC_6H_4$, *i*-Pr)	**2c:** 71 (79)[b]
4	**1d** (*p*-ClC_6H_4, *i*-Pr)	**2d:** 73 (86)[b]
5	**1e** (Ph, *c*-hex)	**2e:** 76 (89)[b]
6	**1f** (*p*-MeC_6H_4, *c*-hex)	**2f:** 68 (76)[b]
7	**1g** (*p*-BrC_6H_4, *c*-hex)	**2g:** 75 (87)[b]
8	**1h** (*p*-FC_6H_4, *c*-hex)	**2h:** 73 (82)[b]
9	**1i** (*p*-$CF_3C_6H_4$, *c*-hex)	**2i:** 77 (86)[b]
10	**1j** (*p*-$MeO_2CC_6H_4$, *i*-Pr)	**2j:** 71 (78)[b]
11	**1k** (*p*-NCC_6H_4, *i*-Pr)	**2k:** 72 (91)[b]
12	**1l** (*p*-$NO_2C_6H_4$, *i*-Pr)	**2l:** 76 (89)[b]
13	**1m** (phenylethenyl, *i*-Pr)	**2m:** 65 (74)[b]
14	**1n** (*m*-BrC_6H_4, *i*-Pr)	**2n:** 64 (70)[b]
15	**1o** (1-naphthyl, *i*-Pr)	**2o:** 78 (86)[b]
16	**1p** (2-phenylethyl, *i*-Pr)	**2p:** 70 (70)[b]
17	**1q** (1-phenylpropyl, *i*-Pr)	**2q:** 63 (75)[b]
18	**1r** (Ph, (*S*)-α-methylbenzyl)	**2r:** 65 (76)[b]
19	**1s** (Ph, *n*-Bu)	**2s:** 71 (77)[b]
20	**1t** (Ph, 2-phenylethyl)	**2t:** 72 (81)[b]
21	**1u** (*n*-$C_{10}H_{21}$, Bn)	**2u:** 74 (87)[b]
22	**1v** (2-thiophenyl, Bn)	**2v:** 65 (80)[b]
23	**1w** (1-adamantyl, Bn)	**2w:** 68 (84)[b]
24	**1x** (piperonyl, Bn)	**2x:** 56 (62)[b]
25	**1y** (Ph, Ph)	**2y:** trace (trace)[b]
26	**1z** (Me, *p*-$MeO_2CC_6H_4$)	**2z:** trace (trace)[b]
27	**1aa** (Ph, *t*-Bu)	**2aa:** trace (trace)[b]

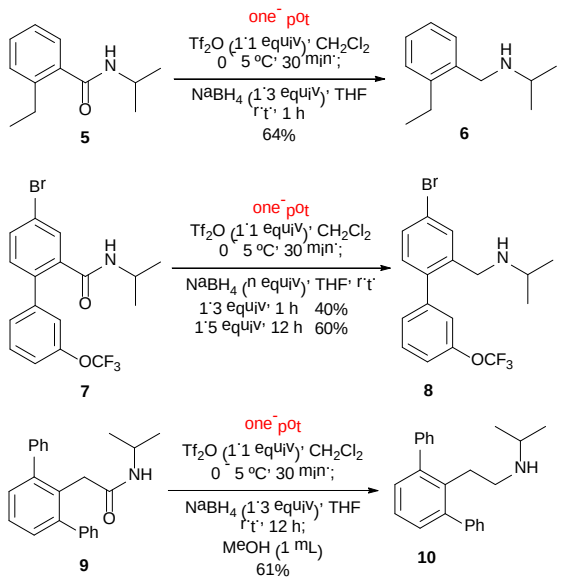
[a] Isolated yield; [b] Yield based on the recovered starting amide.

A change of the *N*-alkyl groups from secondary (*i*-Pr, *c*-hex) to

primary did not affect the reaction (entries 19-20). The reaction of heteroaromatic *N*-benzylthiophene-2-carboxamide **1v** produced amine **2v** in 65% yield (entry 22). Even hindered *N*-benzyladamantane-1-carboxamide **1w** reacted smoothly to give amine **2w** in 68% yield (entry 23). The reaction also tolerated acetal group although the corresponding amine was obtained in a modest yield (56%) (piperonamide **1x**, entry 24). However, the reaction failed with *N*-aryl (entries 25 and 26) and *N*-*tert*-butyl amides (entry 27). Similarly, attempted selective reduction of picolinamides and 2-furoylamide were unsuccessful.

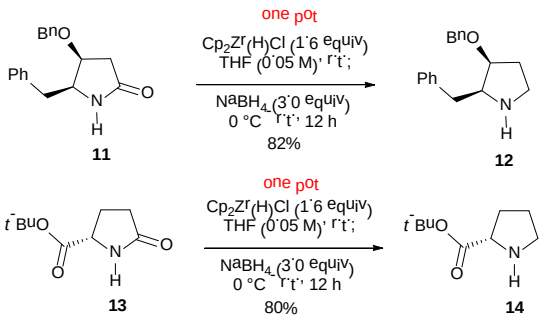
In view of the widespread use of secondary amide as a valuable directing group for both lithiation - functionalization and C-H activation-functionalization, we next focused on the application of the present method to the reduction of C-H functionalization products.

The reduction of a Nakamura's C-H functionalization product **5**[14a] was first investigated. Under the standard conditions (*vide supra*), the reduction of **5** proceeded without incident to give **6** in 64% yield (Scheme 2). It is worth mentioning that amide **5** is also a product obtained by C-H lithiation - ethylation.[13g,h,14a] Comparing with the reaction of the parent amide **1a** (Table 2, entry 1), the lower yield of amine **6** might be attributed to steric hindrance presented in **5**. We next examined the reduction of compound **7**, a Daugulis' C-H functionalization product.[14b] Subjection of **7** to the conditions that we used previously led to the desired amine **8** in 40% yield. To our delight, the yield was improved to 60% by increasing the amount of $NaBH_4$ to 1.5 equiv and prolonging the reduction time to 12 h. Finally, the method was applied to **9**, a Dong's C-H functionalization product.[14c] As expected, under the standard conditions, the reduction of amide **9** gave amine **10** in 61% yield.



Scheme 2 Reduction of selected C-H functionalization products.

We next examined the reduction of secondary lactams. Attempted reduction of secondary lactam **11**, an intermediate in our recent synthesis of alkaloid (–)-streptopyrrolidine,[19] to the optimized reduction conditions failed. This is in agreement with our related results.[15m] The failure let us to call for the chemistry of Ganem, who has demonstrated the selective reduction of secondary lactams (2-pyrrolidones) to imines[15b,c] by Schwartz reagent (Cp_2ZrHCl).[20] It was envisaged that the presumed imine-zirconium complex could be further reduced by $NaBH_4$. To our delight, treatment of lactam **11** with Cp_2ZrHCl in THF at r.t. for 30 min, followed by addition of $NaBH_4$ (3.0 equiv) smoothly afforded pyrrolidine **12** in an 82% yield. Similar reduction of *t*-butyl pyroglutamate **13** produced chemoselectively *t*-butyl prolinate **14** in an 80% yield. The observed chemoselectivity is in agreement with those observed by Ganem.[15d]



Scheme 3

Conclusion

In summary, on the basis of our preliminary results, we have developed a simple method for the direct reduction of secondary amides, which relied solely on two reagents, Tf_2O and $NaBH_4$. Both aromatic and aliphatic amides reacted well, and the *N*-alkyl group can either be primary or secondary alkyls, but the reaction failed with *N*-aryl and *N*-*tert*-butyl amides. The reaction exhibited good functional group tolerance for a series of reducible functional groups ranged from halo (Cl, Br, F) to ether (OMe), from ester (CO_2Me) to cyano (CN), and from nitro (NO_2) to acetal (OCH_2O). The reduction of an α,β-unsaturated amide also ran chemoselectively at the carbonyl group. The reduction method is limited to amides. The chemoselective reduction of secondary lactams has been achieved using Cp_2ZrHCl - $NaBH_4$ combination. The functionalized product may be used for further reactions such as coupling reactions. We also demonstrated that the method is applicable to the direct reduction of C-H lithiation – alkylation and C-H functionalization products. To the best of our knowledge, this is the first example of collective and direct reduction of both C-H lithiation – functionalization and C-H functionalization products, which rends the use of directing group in the chemistry of C-H functionalization more step-economical.

Experimental Section

General Methods

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 (^1H/ 400 MHz, ^{13}C/ 100 MHz) spectrometer. Chemical shifts are expressed in parts per million (δ) relative to an internal standard of residual chloroform (7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR). Data for ^1H NMR are reported as chemical shift (multiplicity, coupling constant, number of proton). ESI-Mass spectra were recorded on a Bruker Dalton ESquire 3000 plus LC-

MS apparatus. Optical rotations were measured with a Perkin-Elmer 341 automatic polarimeter or an Anton Paar MCP 500 polarimeter. Melting points were determined on a Büchi M560 Automatic Melting Point apparatus. Infrared spectra were recorded with a Nicolet Avatar 330 FT-IR spectrometer using film or KBr pellet technique.

Silica gel (300-400 mesh) was used for flash column chromatography, eluting (unless otherwise stated) with ethyl-acetate/ petroleum ether (PE) (60-90°C) mixture. Tf_2O was distilled over phosphorous pentoxide and used within a week. THF was distilled over sodium benzophenone ketyl under N_2. Dichloromethane was distilled over calcium hydride under N_2.

General procedure A for the preparation of amines from amides

To a solution of an amide (1.0 mmol) in anhydrous CH_2Cl_2 (4 mL) was added Tf_2O (1.1 mol equiv, 1.1 mmol) in an ice bath. After being stirred for 0.5 h, $NaBH_4$ (1.3 mol equiv, 1.3 mmol) was added in one portion, and the mixture was diluted with 2.5 mL of THF. The reaction mixture was stirred for 60 min. The reaction was quenched with H_2O (5 mL), and pH of the reaction mixture was adjusted to 10.5-11.0 by addition of a saturated aqueous sodium carbonate solution at 0 °C. The cooled aqueous solution was extracted with Et_2O (5 × 15 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with ethyl acetate/ petroleum ether/ triethylamine (1%) to afford the amine.

General procedure B for the preparation of lactams from amides

A solution of lactam (0.5 mmol) in THF (5 mL) was added dropwise to a suspension of $Cp_2Zr(H)Cl$ (1.6 mol equiv, 0.8 mmol, 206 mg) in THF (5 mL) at room temperature under an argon atmosphere. The mixture was stirred until white suspension disappeared and the solution became clean. Then $NaBH_4$ (3.0 mol equiv, 1.5 mmol) was added in one portion at 0 °C. The mixture was warmed gradually to ambient temperature and stirred overnight. The reaction was quenched with H_2O (2 mL), and the pH of the reaction mixture was adjusted to 10.5-11.0 by addition of a saturated aqueous sodium carbonate solution at 0 °C. The mixture was filtered through a Celite pad (washed with Et_2O). The filtrate was extracted with Et_2O (5 × 10 mL). The combined organic layers were washed with brine (5 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel eluting with ethyl acetate/ petroleum ether to afford the amine.

***N*-Benzylisopropylamine (2a)**

Following the general procedure A, the reduction of amide **1a** (163 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18a] **2a** (138 mg, yield: 74%) a colourless oil. IR (film) ν_{max}: 3448, 2934, 2856, 1615, 1470, 1367, 1113, 707 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.10 (d, J = 6.2 Hz, 6H, CHCH_3), 1.36 (br s, 1H, N*H*), 2.86 (heptet, J = 6.2 Hz, 1H, NHC*H*), 3.78 (s, 2H, CH_2NH), 7.21-7.27 (m, 1H, Ar-*H*), 7.28-7.38 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9 (2C), 48.1, 51.6, 126.8, 128.1 (2C), 128.4 (2C), 140.8 ppm; MS (ESI, *m*/*z*): 150 ($M+H^+$).

***N*-(4-Methylbenzyl)isopropylamine (2b)**

Following the general procedure A, the reduction of amide **1b** (177 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18a] **2b** (110 mg, yield: 67%) as a pale yellow oil. IR (film) ν_{max}: 3457, 2958, 2930, 2858, 1720, 1664, 1612, 1464, 1272, 1105, 823, 754 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.09 (d, J = 6.2 Hz, 6H, CHCH_3), 1.37 (br s, 1H, N*H*), 2.33 (s, 3H, CH_3), 2.84 (heptet, J = 6.2 Hz, 1H, NHC*H*), 3.74 (s, 2H, CH_2NH), 7.12 (d, J = 7.7 Hz, 2H, Ar-*H*), 7.20 (d, J = 7.7 Hz, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 22.9 (2C), 48.0, 51.3, 128.0 (2C), 129.0 (2C), 136.3, 137.7 ppm; MS (ESI, *m*/*z*): 164 ($M+H^+$).

***N*-(4-Methoxybenzyl)isopropylamine (2c)**

Following the general procedure A, the reduction of amide **1c** (193mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18a,b] **2c** (128 mg, yield: 71%) as a pale yellow oil. IR (film) ν_{max}: 3316, 2967, 2930, 2835, 1615, 1507, 1466, 1242, 1176, 1039, 827 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.09 (d, J = 6.3 Hz, 6H, CHCH_3), 1.31 (br s, 1H, N*H*), 2.84 (heptet, J = 6.3 Hz, 1H, NHC*H*), 3.74 (s, 2H, CH_2NH), 3.79 (s, 3H, OCH_3), 6.77-6.94 (m, 2H, Ar-*H*), 7.19-7.25 (m, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9 (2C), 47.9, 51.0, 55.2, 113.7 (2C), 129.2 (2C), 132.9, 158.5 ppm; MS (ESI, *m*/*z*): 180 ($M+H^+$).

***N*-(4-Chlorobenzyl)isopropylamine (2d)**

Following the general procedure A, the reduction of amide **1d** (198 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18a] **2d** (134 mg, yield: 73%) as a pale yellow oil. IR (film) ν_{max}: 3316, 2958, 2926, 2847, 1509, 1470, 1379, 1088, 1010, 806 cm^{-1}; ^1H NMR (CDCl3, 400 MHz): δ 1.09 (d, J = 6.3 Hz, 6H, CHCH_3), 1.30 (br s, 1H, N*H*), 2.83 (heptet, J = 6.3 Hz, 1H, NHC*H*), 3.74 (s, 2H, CH_2NH), 7.19-7.35 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9 (2C), 48.1, 50.8, 128.4 (2C), 129.4 (2C), 132.4, 139.3 ppm; MS (ESI, *m*/*z*): 184 ($M+H^+$).

***N*-Benzylcyclohexylamine (2e)**

Following the general procedure A, the reduction of amide **1e** (203mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12b] **2e** (144 mg, yield: 76%) as a colourless oil. IR (film) ν_{max}: 3312, 3025, 2926, 2851, 1603, 1499, 1458, 1122, 1022, 736, 694 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.10-1.31 (m, 5H, *c*-hex-*H*), 1.36 (br s, 1H, N*H*), 1.57-1.65 (m, 1H, *c*-hex-*H*), 1.69-1.77 (m, 2H, *c*-hex-*H*), 1.90-1.95 (m, 2H, *c*-hex-*H*), 2.45-2.52 (m, 1H, NHC*H*), 3.81 (s, 2H, CH_2NH), 7.21-7.25 (m, 1H, Ar-*H*), 7.31-7.32 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.0 (2C), 26.2, 33.6 (2C), 51.0, 56.2, 126.7, 128.1 (2C), 128.4 (2C), 141.0 ppm; MS (ESI, *m*/*z*): 190 ($M+H^+$).

***N*-[(4-Methylbenzyl)cyclohexylamine (2f)**

Following the general procedure A, the reduction of amide **1f** (218 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12b] **2f** (138 mg, yield: 68%) as a pale yellow oil. IR (film) ν_{max}: 3316, 2922, 2839, 1520, 1449, 1122, 806, 735 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.09-1.29 (m, 5H, *c*-hex-*H*), 1.38 (br s, 1H, N*H*), 1.58-1.64 (m, 1H, *c*-hex-*H*), 1.69-1.76 (m, 2H, *c*-hex-*H*), 1.87-1.94 (m, 2H, *c*-hex-*H*), 2.33 (s, 3H, CH_3), 2.43-2.52 (m, 1H, NHC*H*), 3.76 (s, 2H, CH_2NH), 7.12 (d, *J* = 7.8 Hz, 2H, Ar-*H*), 7.20 (d, *J* = 7.8 Hz, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 21.0, 25.0 (2C), 26.2, 33.5 (2C), 50.7, 56.0, 128.0 (2C), 129.0 (2C), 136.2, 137.9 ppm; MS (ESI, *m*/*z*): 204 ($M+H^+$).

***N*-(4-Bromobenzyl)cyclohexylamine (2g)**

Following the general procedure A, the reduction of amide **1g** (141mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12b] **2g** (101 mg, yield: 75%) as a pale yellow oil. IR (film) ν_{max}: 3303, 2922, 2851, 1478, 1445, 1122, 1072, 806, 737 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.05-1.30 (m, 6H, *c*-hex-*H* and N*H*), 1.60-1.65 (m, 1H, *c*-hex-*H*), 1.69-1.77 (m, 2H, *c*-hex-*H*), 1.84-1.93 (m, 2H, *c*-hex-*H*), 2.41-2.50 (m, 1H, NHC*H*), 3.76 (s, 2H, CH_2NH), 7.17-7.24 (m, 2H, Ar-*H*), 7.41-7.45 (m, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.0 (2C), 26.1, 33.6 (2C), 50.3, 56.1, 120.4, 129.7 (2C), 131.4 (2C), 140.1 ppm; MS (ESI, *m*/*z*): 268 and 270 ($M+H^+$).

***N*-(4-Fluorobenzyl)cyclohexylamine (2h)**

Following the general procedure A, the reduction of amide **1h** (114 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12b] **2h** (76 mg, yield: 73%) as a pale yellow oil. IR (film) ν_{max}: 3299, 2934, 2851, 1611, 1507, 1449, 1221, 1118, 835 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.03-1.33 (m, 6H, *c*-hex-*H* and N*H*), 1.59-1.65 (m, 1H, *c*-hex-*H*), 1.70-1.77 (m, 2H, *c*-hex-*H*), 1.87-1.95 (m, 2H, *c*-hex-*H*), 2.41-2.50 (m, 1H, NHC*H*), 3.77 (s, 2H, CH_2NH), 6.90-7.04 (m, 2H, Ar-*H*), 7.24-7.32 (m, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 25.0 (2C), 26.1, 33.6 (2C), 50.3, 56.2, 115.1 (2C) (d, $^2J_{(C,F)}$ = 21.3 Hz), 129.5 (2C) (d, $^3J_{(C,F)}$ = 8.0 Hz), 136.7, 161.8 (d, $^1J_{(C,F)}$ = 244.4 Hz) ppm; MS (ESI, *m*/*z*): 208 ($M+H^+$).

***N*-(4-(Trifluoromethyl)benzyl)cyclohexylamine (2i)**

Following the general procedure A, the reduction of amide **1i** (136 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12b] **2i** (97 mg, yield: 77%) as a yellow oil. IR (film) ν_{ma}: 3307, 2934, 2868, 1615, 1453, 1325, 1158, 1122, 845, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.03-1.30 (m, 6H, *c*-hex-*H* and N*H*), 1.59-1.67 (m, 1H, *c*-hex-*H*), 1.69-1.79 (m, 2H, *c*-hex-*H*), 1.87-1.96 (m, 2H, *c*-hex-*H*), 2.43-2.52 (m, 1H, NHC*H*), 3.87 (s, 2H, CH_2NH), 7.44 (d, *J* = 8.0 Hz, 2H, Ar-*H*), 7.57 (d, *J* = 8.0 Hz, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.9 (2C), 26.1, 33.6 (2C), 50.5, 56.2, 124.3(d, $^1J_{(C,F)}$ = 271.7 Hz), 125.2 (q, $^3J_{(C,F)}$ = 3.7 Hz) (2C), 128.2 (2C), 129.0 (d, $^2J_{(C,F)}$ = 32.2 Hz), 145.2 ppm; MS (ESI, *m*/*z*): 258 ($M+H^+$).

Methyl 4-((isopropylamino)methyl)benzoate (2j)

Following the general procedure A, the reduction of amide **1j** (221 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **2j** (147 mg, yield: 71%) as a pale yellow oil. IR (film) ν_{max}: 3312, 2971, 2880, 1731, 1603, 1433, 1267, 1105, 1026, 761 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.10 (d, *J* = 6.3 Hz, 6H, CHCH_3), 1.41(br s, 1H, N*H*), 2.84 (heptet, *J* = 6.3 Hz, 1H, NHC*H*), 3.84 (s, 2H, CH_2NH), 3.90 (s, 3H, COOCH_3), 7.40 (d, *J* = 8.0 Hz, 2H, Ar-*H*), 7.99 (d, *J* = 8.2 Hz, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.8 (2C), 48.2, 51.2, 51.9, 127.9 (2C), 128.6, 129.6 (2C), 146.2, 167.0 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{12}H_{18}NO]^+$ ($M+H^+$): 208.1338; found: 208.1336.

4-((Isopropylamino)methyl)benzonitrile (2k)

Following the general procedure A, the reduction of amide **1k** (188 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **2k** (126 mg, yield: 72%) as a pale yellow oil. IR (film) ν_{max}: 3316, 2959, 2929, 2868, 2225, 1608, 1467, 1380, 1174, 1125, 1022, 825 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.10 (d, *J* = 6.2 Hz, 6H, CHCH_3), 1.36 (br s, 1H, N*H*), 2.84 (heptet, *J* = 6.3 Hz, 1H, NHC*H*), 3.85 (s, 2H, CH_2NH), 7.45 (d, *J* = 8.1 Hz, 2H, Ar-*H*), 7.61 (d, *J* = 8.1 Hz, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9 (2C), 48.3, 51.0, 110.6, 119.0, 128.6 (2C), 132.1 (2C), 146.6 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{11}H_{15}N_2]^+$ ($M+H^+$): 175.1235; found: 175.1232.

***N*-(4-Nitrobenzyl)isopropylamine (2l)**

Following the general procedure A, the reduction of amide **1l** (208 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the aqueous ammonia smoked the board), amine **2l** (148 mg, yield: 76%) as a yellow oil. IR (film) ν_{max}: 3316, 2967, 2855, 1611, 1520, 1350, 1101, 802, 736 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.11(d, *J* = 6.3 Hz, 6H, CHCH_3), 1.35 (br s, 1H, N*H*), 2.85 (heptet, *J* = 6.3 Hz, 1H, NHC*H*), 3.90 (s, 2H, CH_2NH), 7.51 (d, *J* = 8.7 Hz, 2H, Ar-*H*), 8.17 (d, *J* = 8.7 Hz, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9, 48.4, 50.8, 123.5, 128.6, 146.9, 148.8 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{10}H_{15}N_2O_2]^+$ ($M+H^+$): 195.1134; found: 195.1135.

(*E*)-*N*-(3-Phenylprop-2-en)isopropylamine (2m)

Following the general procedure A, the reduction of amide **1m** (190 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18d] **2m** (114 mg, yield: 65%) as a pale yellow oil. IR (film) ν_{max}: 3370, 2967, 2922, 2855, 1565, 1458, 1383, 977, 748, 690 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.12 (d, *J* = 6.3 Hz, 6H, CHCH_3), 2.93 (heptet, *J* = 6.3 Hz, 1H, NHC*H*), 3.25 (br s, 1H, N*H*), 3.44 (dd, *J* = 6.5, 1.2 Hz, 2H, CH_2NH), 6.31 (dt, *J* = 15.8, 6.5 Hz, 1H, CH=C*H*CH$_2$), 6.54 (dt, *J* = 15.8, 1.2 Hz, 1H, PhC*H*=CHCH$_2$), 7.18-7.26 (m, 1H, Ar-*H*), 7.27-7.34 (m, 2H, Ar-*H*), 7.34-7.42 (m,

2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.5 (2C), 48.1, 49.1, 126.3 (2C), 127.4, 127.8, 128.5 (2C), 131.7, 137.0 ppm; MS (ESI, *m*/*z*): 176 ($M+H^+$).

***N*-(3-Bromobenzyl)isopropylamine (2n)**

Following the general procedure A, the reduction of amide **1n** (121 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **2n** (73 mg, yield: 64%) as a pale yellow oil. IR (film) ν_{max}: 3324, 3071, 2959, 2927, 2865, 1599, 1569, 1126, 1067, 776, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.10 (d, J = 6.3 Hz, 6H, CHCH_3), 1.42 (br s, 1H, N*H*), 2.84 (heptet, J = 6.3 Hz, 1H, NHC*H*), 3.75 (s, 2H, CH_2NH), 7.15-7.21 (m, 1H, Ar-*H*), 7.22-7.26 (m, 1H, Ar-*H*), 7.34-7.40 (m, 1H, Ar-*H*), 7.46-7.52 (m, 1H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.9 (2C), 48.1, 51.0, 122.5, 126.6, 129.9 (2C), 131.1, 143.3 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{10}H_{15}BrN]^+$ ($M+H^+$): 228.0388 and 230.0367; found: 228.0389 and 230.0369.

***N*-(Naphthalen-1-ylmethyl)isopropylamine (2o)**

Following the general procedure A, the reduction of amide **1o** (214 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18b] **2o** (156 mg, yield: 78%) as a pale yellow oil. IR (film) ν_{max}: 3316, 3045, 2963, 2928, 2868, 2825, 1510, 1467, 1126, 1396, 1171, 802, 792, 777 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.15 (d, J = 6.3 Hz, 6H, CHCH_3), 1.39 (br s, 1H, N*H*), 2.97 (heptet, J = 6.3 Hz, 1H, NHC*H*), 4.21 (s, 2H, CH_2NH), 7.36-7.44 (m, 1H, Ar-*H*), 7.44-7.56 (m, 3H, Ar-*H*), 7.73-7.77 (m, 1H, Ar-*H*), 7.82-7.87 (m, 1H, Ar-*H*), 8.08-8.15 (m, 1H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 23.0 (2C), 48.9, 49.3, 123.5, 125.4, 125.5, 126.0 (2C), 127.6, 128.7, 131.7, 133.8, 136.3 ppm; MS (ESI, *m*/*z*): 200 ($M+H^+$).

***N*-(3-Phenylpropan)isopropylamine (2p)**

Following the general procedure A, the reduction of amide **1p** (191 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[11e] **2p** (124 mg, yield: 70%) as a colourless oil. IR (film) ν_{max}: 3312, 2967, 2835, 1578, 1569, 1112, 1014, 803, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.36 (d, J = 6.5 Hz, 6H, CHCH_3), 2.16-2.25 (m, 2H, CH_2C$H_2$$CH_2$), 2.65 (t, J = 7.5 Hz, 2H, C$H_2$$CH_2$$CH_2$), 2.81-2.87 (m, 2H, CH_2CH_2NH), 3.20 (heptet, J = 6.5 Hz, 1H, NHC*H*), 7.15-7.20 (m, 3H, Ar-*H*), 7.24-7.29 (m, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 19.4 (2C), 27.8, 32.9, 44.3, 50.2, 126.2, 128.3 (2C), 128.5 (2C), 140.1 ppm; MS (ESI, *m*/*z*): 178 ($M+H^+$).

***N*-(3-(2-Phenylbutyl)benzyl)isopropylamine (2q)**

Following the general procedure A, the reduction of amide **1q** (205 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 2), amine **2q** (121 mg, yield: 63%) as a pale yellow oil. IR (film) ν_{max}: 3436, 2958, 2917, 2849, 1578, 1462, 1258, 1114, 1012, 802, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.80 (t, J = 7.5 Hz, 3H), 0.95 (d, J = 6.3 Hz, 3H), 1.00 (d, J = 6.3 Hz, 3H, C$H_3$$CH_2$), 1.19 (br s, 1H, N*H*), 1.51-1.60 (m, 1H, CH_3CH_2), 1.66-1.75 (m, 1H, CH_3CH_2), 2.62-2.78 (m, 3H, CH_2NH and CH_2C*H*CH_2), 2.85-2.93 (m, 1H, NHC*H*), 7.14-7.25 (m, 3H, Ar-*H*), 7.27-7.33 (m, 2H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 12.0, 22.7, 22.8, 27.6, 47.9, 48.5, 53.0, 126.3, 127.8 (2C), 128.4 (2C), 143.8 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{13}H_{22}N]^+$ ($M+H^+$): 192.1752; found: 192.1750.

***(S)*-*N*-Benzyl-*α*-methylbenzylamine (2r)**

Following the general procedure A, the reduction of amide **1r** (225 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18e] **2r** (137 mg, yield: 65%) as a pale yellow oil. IR (film) ν_{max}: 3332, 3029, 2959, 2926, 2843, 1603, 1503, 1449, 1358, 761, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.37 (dd, J = 6.6, 0.8 Hz, 3H, CHCH_3), 1.71 (br s, 1H, N*H*), 3.59 (d, J = 13.1 Hz, 1H, CH_2NH), 3.66 (d, J = 13.1 Hz, 1H, CH_2NH), 3.81 (q, J = 6.7 Hz, 1H, NHC*H*), 7.20-7.40 (m, 10H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.5, 51.6, 57.5, 126.7 (2C), 126.8, 126.9, 128.1 (2C), 128.3 (2C), 128.4 (2C), 140.6, 145.5 ppm; MS (ESI, *m*/*z*): 212 ($M+H^+$).

***N*-Benzyl-*n*-butylamine (2s)**

Following the general procedure A, the reduction of amide **1s** (177 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18f] **2s** (116 mg, yield: 71%) as a pale yellow oil. IR (film) ν_{max}: 3316, 3063, 2955, 2918, 2851, 1603, 1499, 1462, 1130, 740, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.91 (t, J = 7.3 Hz, 3H, CH_2CH_3), 1.30-1.40 (m, 2H, CH_2C$H_2$$CH_3$), 1.43 (br s, 1H, N*H*), 1.46-1.54 (m, 2H, C$H_2$$CH_2$$CH_3$), 2.63 (t, J = 7.3 Hz, 2H, NHC$H_2$$CH_2$), 3.78 (s, 2H, C$H_2$NH), 7.21-7.28 (m, 1H, Ar-*H*), 7.28-7.34 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.0, 20.4, 32.2, 49.2, 54.1, 126.8, 128.1 (2C), 128.3 (2C), 140.5 ppm; MS (ESI, *m*/*z*): 164 ($M+H^+$).

***N*-Benzyl-2-phenethylamine (2t)**

Following the general procedure A, the reduction of amide **1t** (225 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12d] **2t** (153 mg, yield: 72%) as a pale yellow oil. IR (film) ν_{max}: 3324, 3063, 3021, 2926, 2851, 2818, 1599, 1503, 1449, 1122, 1035, 753, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.55 (br s, 1H, N*H*), 2.80-2.86 (m, 2H, $NHCH_2$CH_2), 2.88-2.93 (m, 2H, NHC$H_2$$CH_2$), 3.80 (s, 2H, C$H_2$NH), 7.17-7.25 (m, 4H, Ar-*H*), 7.25-7.33 (m, 6H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.3, 50.5, 53.8, 126.1, 126.9, 128.0 (2C), 128.3 (2C), 128.4 (2C), 128.7 (2C), 140.0, 140.2 ppm; MS (ESI, *m*/*z*): 212 ($M+H^+$).

***N*-Undecyl-benzylamine (2u)**

Following the general procedure A, the reduction of amide **1u** (276 mg, 1.0 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[18d] **2u** (192 mg, yield: 74%) as a colourless oil. IR (film) ν_{max}: 3320, 2934, 2851, 1487, 1458, 1122, 732, 693 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.88 (t, J = 7.0 Hz, 3H, CH_2CH_3), 1.23-1.32 (m, 16H,

$CH_2(CH_2)_8CH_2$), 1.42 (br s, 1H, NH), 1.47-1.54 (m, 2H, $CH_2CH_2CH_3$), 2.62 (t, J = 7.3 Hz, 2H, $NHCH_2CH_2$), 3.78 (s, 2H, $NHCH_2$), 7.22-7.27 (m, 1H, Ar-*H*), 7.32 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.1, 22.7, 27.4, 29.3, 29.6 (4C), 30.1, 31.9, 49.5, 54.1, 126.8, 128.1 (2C), 128.3 (2C), 140.6 ppm; MS (ESI, *m*/*z*): 262 ($M+H^+$).

_N_-(2-Thiophenylmethyl)-benzylamine (2v)

Following the general procedure A, the reduction of amide **1v** (109 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12e] **2v** (66 mg, yield: 65%) as a pale yellow oil. IR (film) ν_{max}: 3320, 3026, 2919, 2849, 1453, 1263, 1107, 735, 699 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.76 (br s, 1H, N*H*), 3.83 (s, 2H, $NHCH_2$), 3.99 (s, 2H, CH_2NH), 6.87-7.00 (m, 2H, Ar-*H*), 7.20-7.28 (m, 2H, Ar-*H*), 7.29-7.39 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 47.5, 52.7, 124.3, 124.8, 126.6, 127.0, 128.2 (2C), 128.4 (2C), 140.0, 144.2 ppm; MS (ESI, *m*/*z*): 204 ($M+H^+$).

_N_-(2-Aamantanylmethyl)-benzylamine (2w)

Following the general procedure A, the reduction of amide **1w** (135 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **2w** (87 mg, yield: 68%) as a pale yellow oil. IR (film) ν_{max}: 3361, 3026, 2905, 2846, 1494, 1452, 1107, 733, 697 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.51-1.55 (m, 6H, $CHCH_2CH$ and N*H*), 1.61-1.67 (m, 4H, $CHCH_2CH$), 1.69-1.74 (m, 3H, $CHCH_2CH$), 1.97 (m, 3H, CH_2CHCH_2), 2.25 (s, 2H, CH_2NH), 3.79 (s, 2H, $NHCH_2$), 7.21-7.26 (m, 1H, Ar-*H*), 7.29-7.35 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 28.5 (3C), 33.5, 37.3 (3C), 40.9 (3C), 54.7, 62.2, 126.7, 127.9 (2C), 128.3 (2C), 141.0 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{18}H_{26}N]^+$ ($M+H^+$): 256.2065; found: 256.2061.

_N_-(2-(Benzo[*d*][1,3]dioxol-5-yl)methyl)- benzylamine (2x)

Following the general procedure A, the reduction of amide **1x** (128 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), the known amine[12e] **2x** (68 mg, yield: 56%) as a pale yellow oil. IR (film) ν_{max}: 3336, 3021, 2916, 2849, 1607, 1501, 1495, 1441, 1246, 807, 736, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.64 (br s, 1H, N*H*), 3.71 (s, 2H, CH_2NH), 3.78 (s, 2H, $NHCH_2$), 5.92 (s, 2H, OCH_2O), 6.73-6.80 (m, 2H, Ar-*H*), 6.86 (s, 1H, Ar-*H*), 7.23-7.28 (m, 1H, Ar-*H*), 7.29-7.37 (m, 4H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 52.9 (2C), 100.8, 108.0, 108.7, 121.2, 126.9, 128.1 (2C), 128.4 (2C), 134.3, 140.3, 146.5, 147.7 ppm; MS (ESI, *m*/*z*): 242 ($M+H^+$).

_N_-(*o*-Ethylbenzyl)isopropylamine (6)

Following the general procedure A, the reduction of amide **5** (96 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **6** (56 mg, yield: 64%) as a pale yellow oil. IR (film) ν_{max}: 3312, 2971, 2934, 2855, 1462, 1453, 1375, 1179, 735 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.12 (d, J = 6.3 Hz, 6H, $CHCH_3$), 1.24 (t, J = 7.6 Hz, 3H, CH_2CH_3), 1.36 (br s, 1H, NH), 2.71 (q, J = 7.6 Hz, 2H, CH_2CH_3), 2.89 (heptet, J = 6.3 Hz, 1H, $NHCH$), 3.77 (s, 2H, CH_2NH), 7.14-7.22 (m, 3H, Ar-*H*), 7.30 (d, J = 7.1 Hz, 1H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 15.4, 23.0 (2C), 25.3, 48.7, 48.8, 125.9, 127.1, 128.5, 128.8, 138.0, 142.2 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{12}H_{20}N]^+$ ($M+H^+$): 178.1596; found: 178.1596.

_N_-[4-Bromo-3'-(trifluoromethoxy)]-[1,1'-biphenyl]-3-yl)methyl)isopropylamine (8)

Following the general procedure A, the reduction of amide **7** (201 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **8** (116 mg, yield: 60%) as a pale yellow oil. IR (film) ν_{max}: 3324, 3054, 2965, 2929, 1610, 1588, 1470, 1375, 1259, 1168, 794, 702, 636 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.96 (d, J = 6.3 Hz, 6H, $CHCH_3$), 1.36 (br s, 1H, N*H*), 2.67 (heptet, J = 6.3 Hz, 1H, $NHCH$), 3.64 (s, 2H, CH_2NH), 7.10 (d, J = 8.1 Hz, 1H, Ar-*H*), 7.22-7.26 (m, 1H, Ar-*H*), 7.28-7.33 (m, 2H, Ar-*H*), 7.41-7.48 (m, 2H, Ar-*H*), 7.64 (m, 1H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.7 (2C), 48.4, 48.7, 119.2, 119.8, 121.6, 121.8, 122.2, 127.4, 129.6, 130.1, 131.4, 132.3, 139.0, 140.3, 142.1, 149.1 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{17}H_{18}BrF_3NO]^+$ ($M+H^+$): 388.0524 and 390.0503; found: 388.0512 and 390.0503.

_N_-((2',6'-Biphenyl)phenethyl)isopropylamine (10)

Following the general procedure A, the reduction of amide **9** (165 mg, 0.5 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 3), amine **10** (96 mg, yield: 61%) as a pale yellow oil. IR (film) ν_{max}: 3328, 3056, 2962, 2867, 1499, 1457, 1171, 760, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.69 (d, J = 6.3 Hz, 6H, $CHCH_3$), 0.91 (br s, 1H, N*H*), 2.28-2.40 (m, 3H, CH_2CH_2 and NH), 2.69-2.76 (m, 2H, CH_2CH_2NH), 7.16-7.22 (m, 2H, Ar-*H*), 7.23-7.29 (m, 1H, Ar-*H*), 7.31-7.44 (m, 10H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 22.6 (2C), 30.9, 47.1, 47.2, 125.3, 126.9 (2C), 128.1 (4C), 129.2 (4C), 129.4 (2C), 135.3 (2C), 142.2 (2C), 142.9 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{23}H_{26}N]^+$ ($M+H^+$): 316.2065; found: 316.2062.

(2*S*,3*S*)-2-Benzyl-3-(benzyloxy)pyrrolidine (12)

Following the general procedure B, the reduction of lactam **11** (100 mg, 0.36 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 5), pyrrolidine **12** (80 mg, yield: 82%) as a colourless oil. $[\alpha]_D^{20}$ +152.7 (*c* 1.0, $CHCl_3$); IR (film) ν_{max}: 3440, 3034, 2926, 2872, 1495, 1453, 1180, 1047, 740, 707 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.84-1.93 (m, 1H, $OCHCH_2CH_2$), 2.00-2.09 (m, 1H, $OCHCH_2CH_2$), 2.87-3.14 (m, 3H, $NHCH_2$ and $PhCH_2CH$), 3.38-3.46 (dd, J = 12.1, 3.1 Hz, 1H, $PhCH_2CH$), 3.46-3.56 (m, 1H, $NHCH$), 3.79 (t, J = 3.4 Hz, 1H, $OCHCH_2$), 3.98 (br s, 1H, N*H*), 4.30 (d, J = 11.3 Hz, 1H, OCH_2CH), 4.50 (d, J = 11.3 Hz, 1H, OCH_2CH), 7.16-7.43 (m, 10H, Ar-*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 27.7, 31.9, 53.0, 70.6, 72.3, 77.7, 126.6, 127.8, 128.0, 128.6 (2C), 129.1, 137.4, 137.9 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_{18}H_{21}NNaO]^+$ ($M+Na^+$): 290.1521; found: 290.1510.

***tert*-Butyl (*S*)-pyrrolidine-2-carboxylate (14)**

Following the general procedure B, the reduction of lactam **13** (100 mg, 0.54 mmol) gave, after chromatographic separation eluting with EtOAc/ PE (*v*/ *v* = 1: 20), the known proline derivative[18g,h] **14** (75 mg, yield: 80%) as a white solid. Mp: 88–89 °C (EtOAc/ hexane); $[\alpha]_D^{20}$ –47.6 (*c* 1.0, $CHCl_3$ {lit.[18i] $[\alpha]_D^{24}$ –40.5 (*c* 0.4, MeOH)}. IR (film) ν_{max}: 3443, 2980, 2930, 1727, 1379, 1180, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 1.49 (s, 9H, C*H*$_3$), 1.75-1.83 (m, 1H, $CH_2CH_2CH_2$), 1.89-1.98 (m, 1H, $CH_2CH_2CH_2$), 2.00-2.11 (m, 1H, CH_2CH_2CH), 2.29-2.41 (m, 1H, CH_2CH_2CH), 2.87-2.98 (m, 1H, CH_2CH_2NH), 3.33-3.42 (m, 1H, CH_2CH_2NH), 3.63-3.71 (m, 1H, COC*H*NH), 4.98 (br s, 1H, N*H*) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 24.8, 27.9 (3C), 30.0, 54.9, 67.3, 83.6, 171.2 ppm; HRMS (ESI, *m*/*z*) calcd for $[C_9H_{17}NNaO_2]^+$ (M+Na^+): 194.1157; found: 194.1150.

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Notes and references

1. For related reviews, see: (a) J. Magano and J. R. Dunetz, *Org. Process Res. Dev.*, 2012, **16**, 1156; (b) M. A. Ricci, Modern Amination Methods; Wiley: New York, 2000; For selected recent examples, see: (c) M. Mewald, J. W. Medley and Movassaghi, M. *Angew. Chem. Int. Ed.*, **2014**, *53*, 11634; (d) S. Bonazzi, B.-C. Cheng, J. S. Wzorek and D. A. Evans, *J. Am. Chem. Soc.*, 2013, **135**, 9338; (e) Y. Tao, D. W. Widlicka, Paul D. Hill, M. Couturier and G. R. Young, *Org. Process Res. Dev.*, 2012, **16**, 1805; (f) Z.-H. Chen, Z.-M. Chen, Y.-Q. Zhang, Y.-Q. Tu and F.-M. Zhang, *J. Org. Chem.*, 2011, **76**, 10173; (g) T. Taniguchi and H. Ishibashi, *Tetrahedron*, 2008, **64**, 8773. (h) A. Deiters, M. Pettersson and S.F. Martin, *J. Org. Chem.*, 2006, **71**, 6547; (i) A. Padwa and J. D. Ginn, *J. Org. Chem.*, 2005, **70**, 5197; (j) Y. Choi, H. Ishikawa, J. Velcicky, G. I. Elliott, M. M. Miller and D. L. Boger, *Org. Lett.*, 2005, **7**, 4539; (k) P. Magnus, L. Gazzard, L. Hobson, A. H. Payne, T. J. Rainey, N. Westlund and V. Lynch, *Tetrahedron*, 2002, **58**, 3423. (l) Y. Nagao, W. M. Dai, M. Ochiai, S. Tsukagoshi and E. Fujita, *J. Org. Chem.*, 1990, **55**, 1148.
2. J. Seyden-Penne, Reductions by Alumino and Borohydrides in Organic Synthesis, 2nd edn., Wiley, New York, 1997.
3. (a) F. Louafi, J. Moreau, S. Shahane, S. Golhen, T. Roisnel, S. Sinbandhit and J. P. Hurvois, *J. Org. Chem.*, 2011, **76**, 9720; (b) P.-Q. Huang, B.-G. Wei and Y.-P. Ruan, *Synlett.*, 2003, 1663; (c) J. C. McWilliams and J. Clardy, *J. Am. Chem. Soc.*, 1994, **116**, 8378; (d) B. Rajashekhar and E. T. Kaiser, *J. Org. Chem.*, 1985, **50**, 5480.
4. (a) H. C. Brown and P. Heim, *J. Org. Chem.*, 1973, **38**, 912; (b) S. Krishnamurthy, *Tetrahedron Lett.*, 1982, **23**, 3315; (c) R. P. Polniaszek and C. R. Kaufman, *J. Am. Chem. Soc.*, 1989, **111**, 4859; (d) M. Bonnat, A. Hercouet and M. Le Corre, *Synth. Commun.*, 1991, **21**, 1579.; see also: (e) A. S. B. Prasad, J. V. B. Kanth and M. Periasamy, *Tetrahedron*, 1992, **48**, 4623; (f) A. Giannis and K. Sandhoff, *Angew. Chem. lnt. Ed. Engl.*, 1989, **28**, 218; (g) P.-Q. Huang, G. Chen and X. Zheng, *J. Heterocyclic Chem.*, 2007, **44**, 499.
5. H. C. Brown, S. Narasimhan and Y. M. Choi, *Synthesis*, 1981, 441.
6. N. Yamazaki, M. Atobe and C. Kibayashi, *Tetrahedron Lett.*, 2001, **42**, 5029.
7. (a) S. J. Paikoff, T. E. Wilson, C. Y. Cho and P. G. Schultz, *Tetrahedron Lett.*, 1996, **37**, 5653; (b) P. J. Brown, K. P. Hurley, L. W. Stuart and T. M. Willson, *Synthesis*, 1997, 778; (c) A. Nefzi, J. M. Ostresh, J. P. Meyer and R. A. Houghten, *Tetrahedron Lett.*, 1997, **38**, 931; (d) D. G. Hall, C. Laplante, S. Manku, and J. Nagendran, *J. Org. Chem.*, 1999, **64**, 698; (e) M. Couturier, J. L. Tucker, B. M. Andresen, P.l Dubé and J. T. Negri, *Org. Lett.*, 2001, **3**, 465; (f) S. Manku , C. Laplante , D. Kopac , T.y Chan and D. G. Hall, *J. Org. Chem.*, 2001, **66**, 874.
8. (a) H. Akamatsu, S. Kusumoto and K. Fukase, *Tetrahedron Lett.*, 2002, **43**, 8867; (b) B. Thiedemann, C. M. L. Schmitz and A. Staubitz. *J. Org. Chem.*, **2014**, *79*, pp 10284.
9. (a) M. A. Mauragis, M. F. Lipton and M. F. Veley, *Org. Proc. Res. Dev.*, 2002, **6**, 192; (b) Stepwise: B. H. Lee and M. F. Clothier, *Tetrahedron Lett.*, 1999, **40**, 643.
10. For recent reviews, see: (a) A. M. Smith and R. Whyman, *Chem. Rev.*, 2014, **114**, 5477; (b) S. Werkmeister, K. Junge and M. Beller, *Org. Process Res. Dev.*, 2014, **18**, 289; (c) P. A. Dub and T. Ikariya, *Adv. Synth. Catal.*, 2012, **2**, 1718; (d) D. Addis, S. Das, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2011, **50**, 6004; (e) S. Das, S. Zhou, D. Addis, K. Junge, S. Enthaler and M. Beller, *Top. Catal.*, 2010, **53**, 979; (f) Modern Reduction Methods; P. G. Andersson and I. J. Munslow, Eds.; Wiley: New York, 2008; For selected examples on the reduction of tertiary amides, see: (g) M. Igarashi and T. Fuchikami, *Tetrahedron Lett.*, 2001, **42**, 1945; (h) N. Sakai, K. Fujii and T. Konakahara, *Tetrahedron Lett.*, 2008, **49**, 6873; (i) G. Barbe and A. B. Charette, *J. Am. Chem. Soc.*, 2008, **130**, 18; (j) S. -L. Zhou, K. Junge, D. Addis, S. Das and M. Beller, *Angew. Chem. Int. Ed.*, 2009, **48**, 9507; (k) Y. Sunada, H. Kawakami, T. Imaoka, Y. Motoyama and H. Nagashima, *Angew. Chem. Int. Ed.*, 2009, **48**, 9511; (l) S. Hanada, E. Tsutsumi, Y. Motoyama and H. Nagashima, *J. Am. Chem. Soc.*, 2009, **131**, 15032; (m) S. Das, D. Addis, S. -L. Zhou, K. Junge and M. Beller, *J. Am. Chem. Soc.*, 2010, **132**, 1770 (correction: *J. Am. Chem. Soc.*, 2010, **132**, 4971); (n) S.-H. Xiang, J. Xu, H.-Q. Yuan and P.-Q. Huang, *Synlett*, 2010, 1829; (o) M. Stein and B. Breit, *Angew. Chem. Int. Ed.*, 2013, **52**, 2231; (p) W.-L. Xie, M.-D. Zhao and C.-M. Cui, *Organometallics*, 2013, **32**, 7440; (q) E. Blondiaux and T. Cantat, *Chem. Commun.*, 2014, **50**, 9349; (r) J. D. Kirkham, R. J. Butlin and J. P. Harrity *Angew. Chem. Int. Ed.*, **2012**, *51*, 6402.
11. For selected recent examples on the reduction of secondary amides, see: (a) Y. Motoyama, K. Mitsui, T. Ishida and H. Nagashima, *J. Am. Chem. Soc.*, 2005, **127**, 13150; (b) T. Ohta, M. Kamiya, M. Nobutomo, K. Kusui and I. Furukawa, *Bull. Chem. Soc. Jpn.*, 2005, **78**, 1856; (c) A. C. Fernandes and C. C. Romão, *J. Mol. Cat. A: Chem.*, 2007, **272**, 60; (d) A. A. Núñez Magro, G. R. Eastham and D. J. Cole-Hamilton, *Chem. Commun.*, 2007, 3154; (e) S. Hanada, T. Ishida, Y. Motoyama and Nagashima, H. *J. Org. Chem.*, 2007, **72**, 7551; For two early examples, see: (f) Atta-ur-Rahman, A. Basha, N. Waheed and S. Ahmed, *Tetrahedron Lett.*, 1976, **17**, 219; (g) R. F. Borch, *Tetrahedron Lett.*, 1968, **9**, 61.
12. (a) E. A. Voight, M. S. Bodenstein, N. Ikemoto and M. H. Kress, *Tetrahedron Lett.*, 2006, **47**, 1717; (b) G. Pelletier, W. S. Bechara and A. B. Charette, *J. Am. Chem. Soc.*, 2010, **132**, 12817; (c) S. Das, D. Addis, K Junge and M. Beller, *Chem. Eur. J.*, 2011, **17**, 12186; (d) S. Das, B. Join, K. Junge and M. Beller, *Chem. Commun.*, 2012, **48**, 2683; (e) C. Cheng and M. Brookhart, *J. Am. Chem. Soc.*, 2012, **134**, 11304; (f) J. T. Reeves, Z. Tan, M. A. Marsini, Z. S. Han, Y. Xu, D. C. Reeves, H. Lee, B. Z. Lu and C. H. Senanayake, *Adv. Synth. Catal.*, 2013, **355**, 47; (g) T. Zhang, Y. Zhang, W. Zhang and M. Luo, *Adv. Synth. Catal.*, 2013, **355**, 2775; (h) B. Ravinder, S. R. Reddy, A. P. Reddy and R. Bandichhor, *Tetrahedron Lett.*, 2013, **54**, 4908; (i) J. A. M. de L. Torre, K. Grabow, U. Bentrup, K. Junge, S. Zhou, A. Brückner and M. Beller, *Angew. Chem. Int. Ed.*, 2013, **52**, 11577;
13. For a review on the use of secondary amide as a directing group for lithiation, see: (a) P. Beak, A. Basu, D. J. Gallagher, Y. S. Peak and S. Thayumanavan, *Acc. Chem. Res.*, 1996, **29**, 552; for selected examples, see: (b) P. Beak and D. J. Kempf, *J. Am. Chem. Soc.*, 1980, **102**, 4550; (c) P. Beak, D. J. Kempf and K. D. Wilson, *J. Am. Chem. Soc.*, 1985, **107**, 4745; (d) D. A. Evans and G. C. Fu, *J. Am. Chem. Soc.*, 1991, **113**, 4042; (e) G. P. Lutz, H. Du, D. J. Gallagher and P. Beak, *J. Org. Chem.*, 1996, **61**, 4542; (f) D. J. Pippel, M. D. Curtis, H. Du and P. Beak, *J. Org. Chem.*, 1998, **63**, 2; (g) J. M. Laumer, D. D. Kim and P. Beak, *J. Org. Chem.*, 2002, **67**, 6797; (h) K. Smith, G. A. El-Hiti and M. B. Alshammari, *J. Org. Chem.*, 2012, **77**, 11210.
14. (a) Q. Chen, L. Ilies, N. Yoshikai and Eiichi Nakamura, *Org. Lett.*, 2011, **13**, 3232; (b) D. Shabashov and O. Daugulis, *Org. Lett.*, 2006, **8**, 4947; (c) C. S. Yeung, X. Zhao, N. Borduas and V. M. Dong,

Chem. Sci., 2010, **1**, 331.

15. For selected direct transformation of secondary amides, see: (a) N. J. Sisti, F. W. Fowler and D. S. Grierson, *Synlett*, 1991, 816; (b) D. J. A. Schedler, A. G. Godfrey, and B. Ganem, *Tetrahedron Lett.*, 1993, **34**, 5035; (c) D. J. A. Schedler, J. Li and B. Ganem, *J. Org. Chem.*, 1996, **61**, 4115; (d) Q. Xia and B. Ganem, *Org. Lett.*, 2001, **3**, 485; (e) Q. Xia and B. Ganem, *Tetrahedron Lett.*, 2002, **43**, 1597. (f) M. Movassaghi and M. D. Hill, *J. Am. Chem. Soc.*, 2006, **128**, 4592; (g) J. T. Spletstoser, J. M. White, A. R. Tunoori and G. I. Georg, *J. Am. Chem. Soc.*, 2007, **129**, 3408; (h) H.-B. Zhou, G.-S. Liu and Z.-J. Yao, *J. Org. Chem.*, 2007, **72**, 6270; (i) S.-L. Cui, J. Wang and Y.-G. Wang, *J. Am. Chem. Soc*., 2008, **130**, 13526. (j) Y. Oda, T. Sato and N. Chida, *Org. Lett*., 2012, **14**, 950; (k) W. S. Bechara, G. Pelletier and A. B. Charette, *Nat. Chem.*, 2012, **4**, 228; (l) K.-J. Xiao, A.-E. Wang, Y.-H. Huang and P.-Q. Huang, *Asian J. Org. Chem.*, 2012, **1**, 130; (m) K.-J. Xiao, A.-E Wang, Y.-H. Huang and P.-Q. Huang, *Acta Chim. Sinica*., 2012, **70**, 1917; (n) K.-J. Xiao, A.-E Wang and P.-Q. Huang, *Angew. Chem. Int. Ed.*, 2012, **51**, 8314; (o) Y. Gao, Z. Huang, R. Zhuang, J. Xu, P. Zhang, G. Tang, and Y. Zhao, *Org. Lett.*, **2013**, *15*, 4214. (p) K. Shirokane, T. Wada, M. Yoritate, R. Minamikawa, N. Takayama, T. Sato and N. Chida, *Angew. Chem. Int. Ed.*, 2014, **53**, 512; (q) M. Szostak, M. Spain, A. J. Eberhart and D. J. Procter, *J. Am. Chem. Soc*., 2014, **136**, 2268; (r) T. Sato and N. Chida, *Org. Biomol. Chem.*, 2014, **12**, 3147; (s) M. Yoritate, T. Meguro, N. Matsuo, K. Shirokane, T. Sato and N. Chida, *Chem. Eur. J.*, 2014, **20**, 8210. (t) M. Nakajima, Y. Oda, T. Wada, R. Minamikawa, K. Shirokane, T. Sato and N. Chida, *Chem. Eur. J.*, 2014, DOI: 10.1002/chem.201404648.

16. (a) K.-J. Xiao, J.-M. Luo, K.-Y. Ye, Y. Wang and P.-Q. Huang, *Angew. Chem. Int. Ed*., 2010, **49**, 3037; (b) K.-J. Xiao, Y. Wang, K.-Y. Ye and P.-Q. Huang, *Chem. Eur. J.*, 2010, **16**, 12792; (c) S.-Y. Huang, Z. Chang, S.-C. Tuo, L.-H. Gao, A.-E Wang and P.-Q. Huang, *Chem. Commun.*, 2013, **49**, 7088; (d) K.-J. Xiao, Y. Wang, Y.-H. Huang, X.-G. Wang, J.-C. Liao and P.-Q. Huang, *J. Org. Chem.*, 2013, **78**, 8305; (e) K.-J. Xiao, J.-M. Luo, X.-E. Xia, Y. Wang and P.-Q. Huang, *Chem. Eur. J.*, 2013, **19**, 13075; (f) P.-Q. Huang, W. Ou, K.-J. Xiao and A.-E Wang, *Chem. Commun.*, 2014, **50**, 8761; (g) H.-Q. Deng, X.-Y. Qian, Y.-X. Li, J.-F. Zheng, L.-F. Xie and P.-Q. Huang, *Org. Chem. Front.*, 2014, **1**, 258.

17. For reviews on the chemistry of triflic acid and its derivatives, see: (a) P. J. Stang, M. Hanack and M. L. R. Subramanian, *Synthesis*, 1983, 85; (b) I. L. Baraznenok, V. G. Nenajdenko and E. S. Balenkova, *Tetrahedron*, 2000, **56**, 3077; For selected recent examples on the use of Tf_2O as a powerful amide activator for a variety of transformations, see: (c) G. Bélanger, R. Larouche-Gauthier, F. Ménard, M. Nantel and F. Barabé, *J. Org. Chem.*, 2006, **71**, 704; (d) B. Peng, X. Huang, L.-G. Xie and N. Maulide, *Angew. Chem. Int. Ed.*, 2014, **53**, 8718; (e) B. Peng, D. Geerdink, C. Farès and N. Maulide, *Angew. Chem. Int. Ed.*, 2014, **53**, 5462.

18. (a) O. Saidi, A. J. Blacker, M. M. Farah, S. P. Marsden and J. M. J. Williams, *Angew. Chem. Int. Ed.*, 2009, **48**, 7375; (b). S. W. C. Bornschein, K. Junge and M. Beller, *Eur. J. Org. Chem.*, 2013, 3671; (c) N. Fleury-Brgeot, J. Raushel, D. L. Sandrock, S. D. Dreher and G. A. Molander, *Chem. Eur. J.*, 2012, **18**, 9564; (d) R. A. Sanchez-Delgado, R. G. D. Rosa and E. Ocando-Mavarezc, *J. Mol. Cat. A*, 1996, **108**, 125; (e) C. Guérin, V. Bellosta, G. Guillamot and J. Cossy, *Org. Lett.*, 2011, **13**, 3534; (f) W. Zhang, X. Dong and W. Zhao. *Org. Lett.*, 2011, **13**, 5386; (g) A. H. G. Siebum, R. K. F. Tsang, R. van der Steen, J. Raap and J. Lugtenburg**,** *Eur. J. Org. Chem.*, 2004, 4391; (h) S. Tanaka, H. Saburi, T. Murase, M. Yoshimura and M. Kitamura, *J. Org. Chem.*, 2006, **71**, 4682; (i) G. Jolles, G. Poiget, J. Robert, B. Terlain and J. P. Thomas, *Bull. Soc. Chim. Fr*., 1965, **8**, 2252.

19. S.-H. Xiang, H.-Q. Yuan and P.-Q. Huang, *Tetrahedron: Asymmetry*, 2009, **20**, 2021.

20. (a) J. Schwartz and J. A. Labinger, *Angew. Chem., Int. Ed. Engl.* 1976, **15**, 333; (b) B. Ganem and R. R. Franke, *J. Org. Chem.* 2007, **72**, 3981.