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EFFICIENT SYNTHESIS OF *N*-METHYLAMIDES AND AMINES VIA 4-(ALKYLAMINO)BENZYL-*N*-METHYLAMINE AS A NEW PROTECTING GROUP

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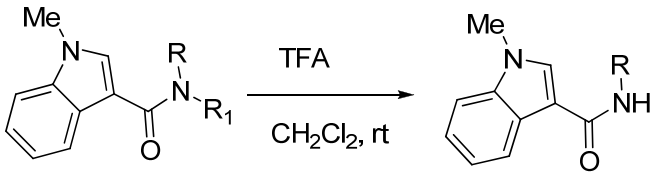
Abstract – 4-(Alkylamino)benzyl-*N*-methylamine is a good protecting group for the synthesis of *N*-methylamides and amines. The *N*-debenzylation of *N*-methylamides and amines can be carried out selectively and efficiently under condition using trifluoroacetic acid (TFA).

Amines are important functionalities in various natural products. Due to its unique biological properties, the amine moiety plays a central role in important pharmacophores.[1] Considering their numerous applications in the fields of pharmacology, biology and organic chemistry, there are continuous needs for efficient synthetic methods for their derivatives.[1,2] Especially the synthesis of *N*-methylamine is of great interest in organic chemistry. General synthetic methods for the preparation of *N*-methylamines include direct *N*-methylation,[3] *N*-methylation of carbamate derivatives,[4] the use of *N*-methylbenzylamine[5] or reductive amination protocol.[6] *N*-Methylation of amide and amine is usually carried out by the treatment of an amine with a methyl halide in the presence of a base. However, selective synthesis of *N*-methylation is often complex due to the difficulty of preventing the formation of the corresponding *N,N*-dimethylation.[3] So it is general that the *N*-methyl functionality of *N*-methylamide and amine is introduced from *N*-methylbenzylamine and the benzyl group is removed afterward. *N*-Methylbenzylamine is used for the synthesis of selectively monomethylated products.[5] Unfortunately, the use of *N*-benzyl groups has problems because their removal is often difficult.[7] There are numerous procedures in the literature which describe a variety of cleavage and *N*-deprotection methods for amine and amide synthesized with the *N*-benzyl groups strategy. The most common method of removal is the use of

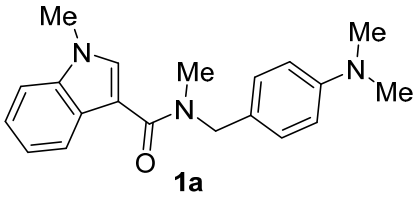
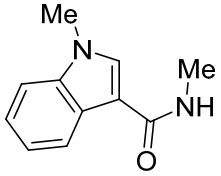
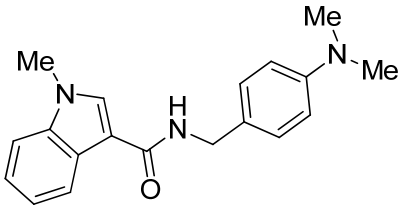
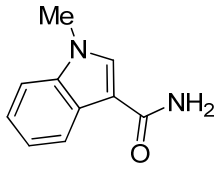
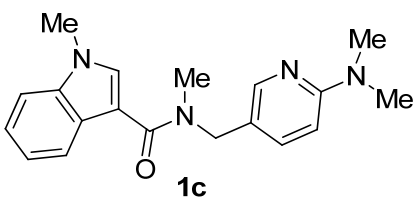
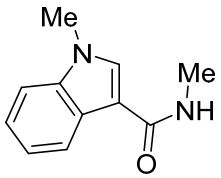
hydrogenolysis with catalytic Pd/C,[8] or strongly reductive conditions, such as $Na/NH_3(l)$[9] or Li.[10] These conditions can limit the use of *N*-benzyl protecting groups for unstable compounds. Many studies have been conducted to develop more efficient *N*-debenzylation conditions and *N*-protecting groups.

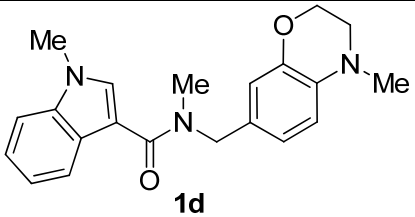
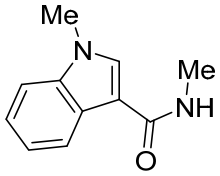
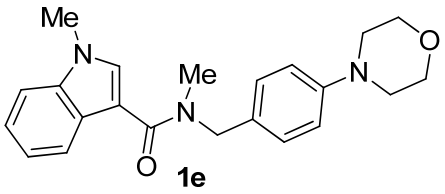
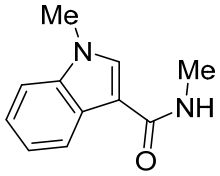
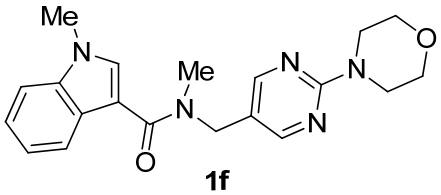
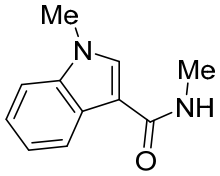
We report the use of 4-(alkylamino)benzylamines as convenient and effective protecting groups. The application of these reagents is summarized in **Table 1**. A series of six 4-(alkylamino)benzylamides were synthesized by the reaction of the corresponding carboxylic acids with 4-(alkylamino)benzylamines in the presence of *O*-benzotriazole-*N,N,N′,N′*-tetramethyl-uronium-hexafluorophosphate (HBTU) at ambient temperature with good yields produced.[11] The *N*-debenzylation method was used with TFA. This reaction condition produced an efficient and selective deprotection of 4-(alkylamino)benzylamides. The results are summarized in **Table 1**.

Table 1. Results of deprotection of the 4-(alkylamino)benzylamides



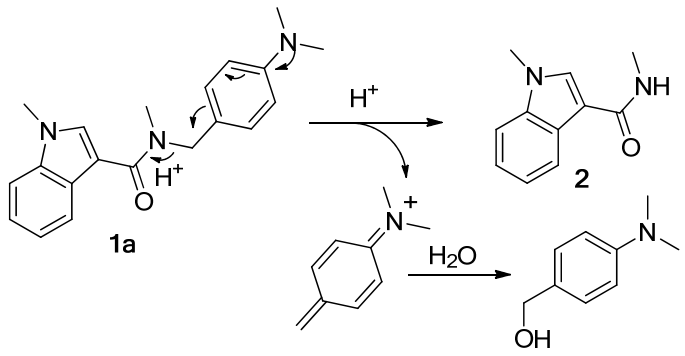
1 **2**

entry	substrate	product	yield (%)[a]
1	 **1a**	 **2a**	80
2	 **1b**	 **2b**	no reaction
3	 **1c**	 **2a**	no reaction

4	 **1d**	 **2a**	77
5	 **1e**	 **2a**	75
6	 **1f**	 **2a**	no reaction

[a] Isolated yield

As shown in entries 1, 4 and 5, the *N*-debenzylation reaction gave corresponding *N*-methylamines in good yields. None of the established methods was useful for entries 2, 3 and 6, and product formation was not observed even after prolonged reaction (20 h). In entry 2, it is well known that the electron-donating methyl can increase the negative charge population on the nitrogen atom in amine molecules (i.e. NH is less reactive than NHMe). The *N*-debenzylation of *N*-methylamide and amide can be carried out selectively. In entries 3 and 6, it is difficult for electrons to move through a benzene ring because of the heteroatom, which prevents deprotection. 4-(Alkylamino)benzylamides are expected to undergo *N*-debenzylation with TFA through the initial protonation of nitrogen atom of the weakly basic amide (Scheme 1).

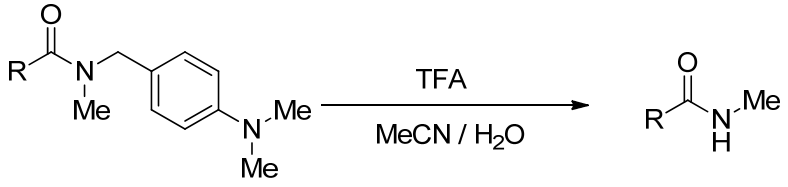


Scheme 1. Proposed mechanism for deprotection of 4-(alkylamino)benzylamide

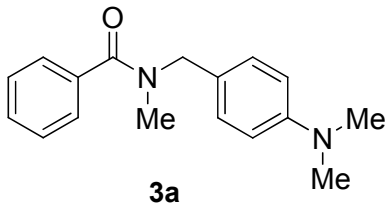
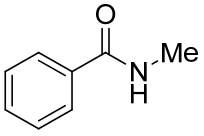
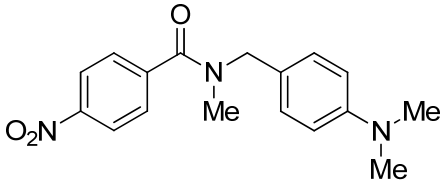
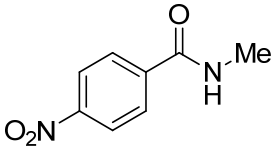
4-(Alkylamino)benzyl groups can be cleaved with TFA in CH_2Cl_2 at ambient temperature and also produce good protecting groups for amide. Among them, 4-(dimethylamino)benzyl-*N*-methylamine was selected as the protecting group of other amides and arylamines due to its convenience and low cost. We hope to investigate the possibility of applying 4-(dimethyl-amino)benzyl-*N*-methylamine to other amides and amines.

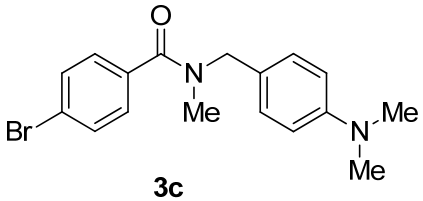
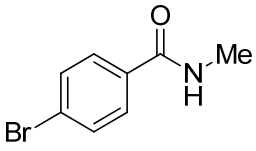
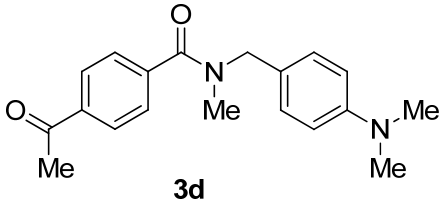
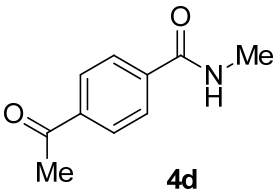
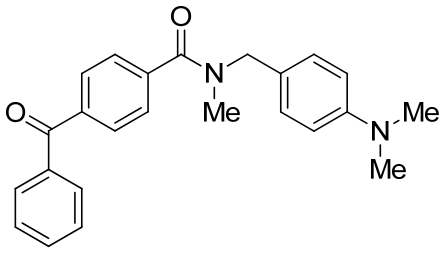
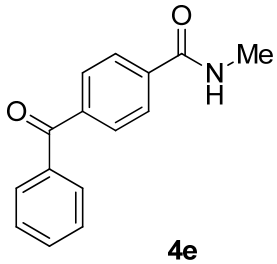
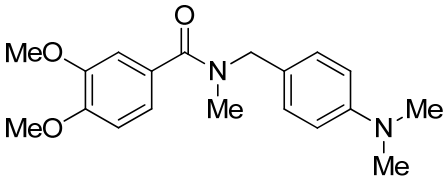
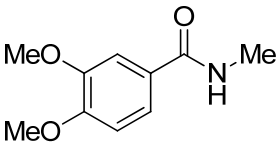
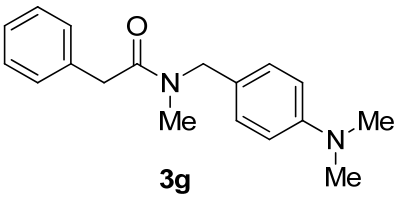
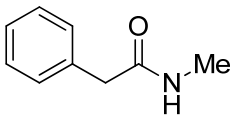
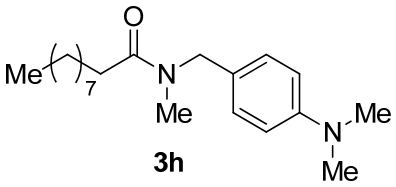
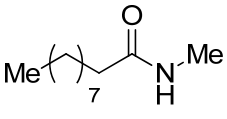
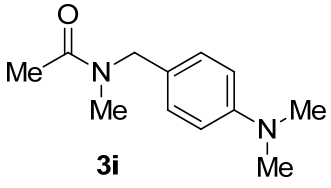
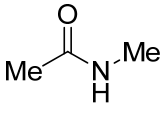
A series of nine 4-(dimethylamino)benzyl-*N*-methylamides (**3a-i**) were synthesized by the reaction of the corresponding carboxylic acids with 4-(dimethylamino)benzyl-*N*-methylamines in the presence of HBTU at ambient temperature, producing good yields. The *N*-debenzylation method was used with TFA. In case of amides and amines except indoleamides, the reaction was not progressed at rt. So, we carried out the reaction of amides and amines except indoleamides in MeCN-H_2O at 80~100 ^oC because of the reactivity. The *N*-debenzylation results are shown in **Table 2**. As shown in entries 1-9, the debenzylation reactions were rapid and produced *N*-methylamines (**4a-i**) in good yields. A variety of amides were applicable to the reaction condition.

Table 2. Results of deprotection of the 4-(dimethylamino)benzyl-*N*-methylamides



3 **4**

entry	substrate	product	temp. (^oC)	time (h)	yield (%)[a]
1	 **3a**	 **4a**	80	2	72
2	 **3b**	 **4b**	80	2	80

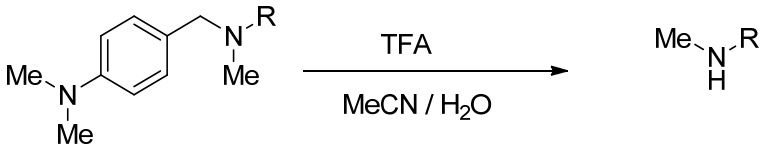
3	 **3c**	 **4c**	80	2	72
4	 **3d**	 **4d**	80	2	75
5	 **3e**	 **4e**	80	2	70
6	 **3f**	 **4f**	80	2	75
7	 **3g**	 **4g**	100	2	88
8	 **3h**	 **4h**	100	2	76
9	 **3i**	 **4i**	100	2	65

[a] Isolated yield

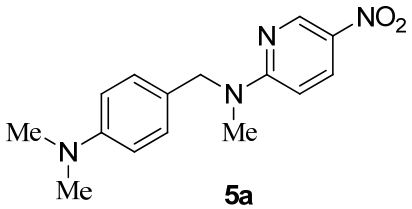
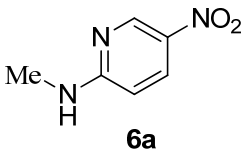
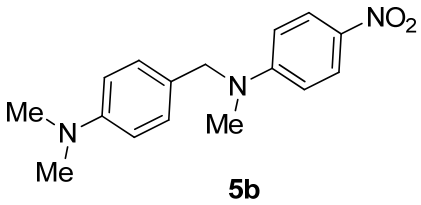
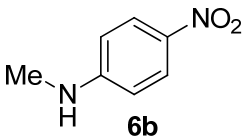
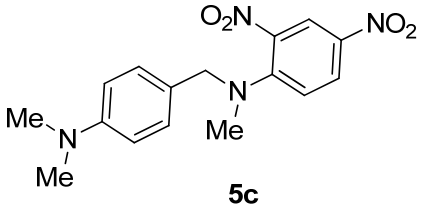
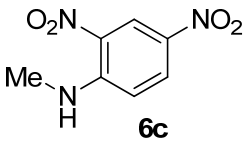
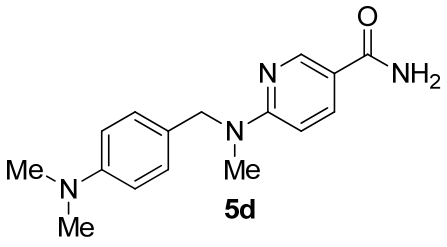
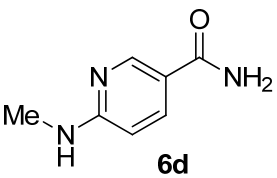
As shown in entries 1-5, 4-(dimethylamino)benzyl-*N*-methylarylamines (**5a-e**) were synthesized by the reaction of addition-elimination with 4-(dimethylamino)benzyl-*N*-methylamine, with good yields. As shown in entries 6-8, 4-(dimethylamino)benzyl-*N*-methyl aliphatic amines (**5f-h**) were synthesized by the reaction of 4-(dimethylamino)benzyl-*N*-methylamine and aliphatic halides, with good yields.

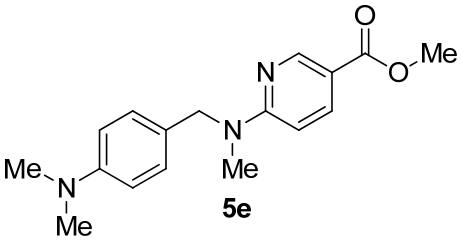
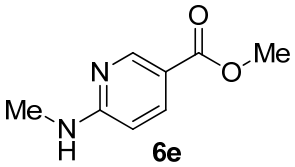
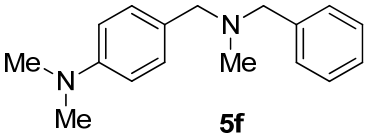
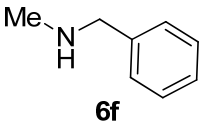
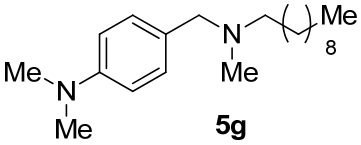
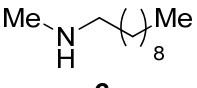
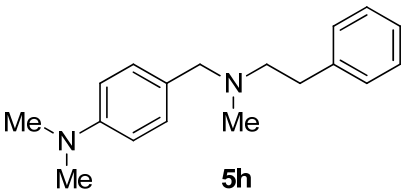
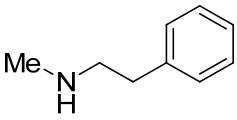
The *N*-debenzylation reaction of 4-(dimethylamino)benzyl-*N*-methylarylamines and aliphatic amines was examined by the use of TFA / MeCN / H_2O at 80~120 °C, and the results are shown in **Table 3**. The yields of *N*-debenzylation reaction (**6a-h**) were good as shown in entries 1-8.

Table 3. Results of deprotection of the 4-(dimethylamino)benzyl-*N*-methylarylamines and aliphatic amines



5 **6**

entry	substrate	product	temp. (°C)	time (h)	yield (%)[a]
1	 **5a**	 **6a**	80	5	75
2	 **5b**	 **6b**	80	5	91
3	 **5c**	 **6c**	80	5	67
4	 **5d**	 **6d**	80	5	71

5	 **5e**	 **6e**	80	5	80
6	 **5f**	 **6f**	120	5	70
7	 **5g**	 **6g**	120	5	82
8	 **5h**	 **6h**	120	5	75

[a] Isolated yield

In conclusion, we report 4-(alkylamino)benzylamines as convenient and effective protecting groups. The *N*-debenzylation of *N*-methylamides and amines were carried out selectively and efficiently with the use of TFA. This procedure is very useful for synthesizing a wide variety of nitrogen-containing amides and arylamines, and can be applied to a variety of functional groups. The application of this methodology can afford high chemical yields.

EXPERIMENTAL

General: Commercially available reagents were used without additional purification, unless otherwise stated. All reactions were performed under an inert atmosphere of nitrogen. Nuclear magnetic resonance spectra (^{1}H and ^{13}C NMR) were recorded on a Bruker Unity 400 MHz spectrometer for $CDCl_3$ solutions and chemical shifts are reported as parts per million (ppm) relative to, respectively, residual $CHCl_3$ δ H (7.26 ppm) and $CDCl_3$ δ C (77.0 ppm) as internal standards. Resonance patterns are reported with the notations *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *dd* (doublet of doublet), *td* (triplet of doublet), and *m* (multiplet). In addition, the notation br is used to indicate a broad signal. Coupling constants (*J*) are reported in hertz (Hz). IR spectra were recorded on a Bruker Vector IFS-66. Infrared spectrophotometer is reported as cm^{-1}. Thin layer chromatography was carried out using plates coated with Kieselgel 60F254

(Merck). For flash column chromatography, E. Merck Kieselgel 60 (230-400 mesh) was used. HPLC-Mass spectra (LC/MS) were recorded on a Waters 2767 LC/MS System. High-resolution mass spectra (HRMS) were recorded on a JEOL, JMS-700 spectrometer.

Typical procedure for the syntheses of 4-(alkylamino)benzylamides.

To a solution of carboxylic acid (0.285 mmol) in anhydrous DMF (1 mL) were added HBTU (130 mg, 0.342 mmol) and DIPEA (0.119 mL, 0.684 mmol) at 25 ^{o}C. The reaction mixture was stirred at 25 ^{o}C for 30 min and then 4-(alkylamino)benzylamine (0.342 mmol) was added at 25 ^{o}C. The reaction mixture was stirred at 80 ^{o}C for 8 h and then cooled to 25 ^{o}C. The reaction mixture was treated with water (50 mL) and the product extracted into Et_2O (50 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography (*n*-hexane / CH_2Cl_2 = 10 / 90).

***N*-(4-(Dimethylamino)benzyl)-*N*,1-dimethyl-1*H*-indole-3-carboxamide (1a)**; Yield 85%; as a yellow oil; IR (KBr) ν_{max} 3358, 2947, 2833, 1665, 1452, 1115, 1032, 658 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.0 Hz, 1H), 7.18~7.36 (m, 6H), 6.73 (d, *J* = 8.4 Hz, 2H), 4.72 (s, 2H), 3.78 (s, 3H), 3.08 (s, 3H), 2.95 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 150.0, 136.5, 130.5, 129.2, 128.6, 127.0, 125.2, 122.4, 121.4, 120.9, 112.8, 112.7, 109.5, 40.7, 33.1; HRMS (EI$^+$) Calcd for $C_{20}H_{23}N_3O$ $[M]^+$ 321.1837, found 321.1841.

***N*-(4-(Dimethylamino)benzyl)-1-methyl-1*H*-indole-3-carboxamide (1b)**; Yield 75%; as a white solid; mp 156 ^{o}C; IR (KBr) ν_{max} 3358, 2946, 2833, 1665, 1452, 1115, 1032, 694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.92 (d, *J* = 7.6 Hz, 1H), 7.65 (s, 1H), 7.18~7.36 (m, 5H), 6.72 (d, *J* = 8.8 Hz, 2H), 6.05 (br, 1H), 4.60 (d, *J* = 5.2 Hz, 2H), 3.81 (s, 3H), 2.95 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 164.9, 137.6, 132.3, 129.1, 125.4, 122.5, 121.4, 120.2, 112.9, 111.0, 43.3, 40.7, 33.3; HRMS (EI$^+$) Calcd for $C_{19}H_{21}N_3O$ $[M]^+$ 307.1682, found 307.1685.

***N*-((6-(Dimethylamino)pyridin-3-yl)methyl)-*N*,1-dimethyl-1*H*-indole-3-carboxamide (1c)**; Yield 80%; as a yellow oil; IR (KBr) ν_{max} 3358, 2946, 2833, 1665, 1452, 1115, 1032, 748 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 8.09 (s, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.48 (m, 1H), 7.38 (s, 1H), 7.18~7.35 (m, 3H), 6.51 (d, *J* = 8.8 Hz, 1H), 3.81 (s, 3H), 4.65 (s, 2H), 3.09 (s, 6H), 3.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* 167.5, 136.5, 130.8, 126.7, 122.5, 121.2, 120.9, 110.6, 109.6, 106.1, 38.2, 33.2; HRMS (EI$^+$) Calcd for $C_{19}H_{22}N_4O$ $[M]^+$ 322.1795, found 322.1794.

***N*,1-Dimethyl-*N*-((4-methyl-3,4-dihydro-2*H*-benzo[*b*][1,4]oxazin-7-yl)methyl)-1*H*-indole-3-carboxamide (1d)**; Yield 81%; as a yellow oil; IR (KBr) ν_{max} 3380, 2947, 2833, 1660, 1453, 1116, 1032, 659 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 7.86 (d, *J* = 8.0 Hz, 1H), 7.18~7.36 (m, 4H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.70 (s, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 4.65 (s, 2H), 4.30 (t, *J* = 4.4 Hz, 2H), 3.77 (s, 3H), 3.25 (t, *J* = 4.4 Hz, 2H),

3.04 (s, 3H), 2.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 144.5, 136.5, 135.9, 130.6, 127.4, 127.0, 122.4, 121.4, 120.9, 112.7, 109.5, 65.0, 50.9, 49.2, 38.9, 33.1; HRMS (EI^+) Calcd for $C_{21}H_{23}N_3O_2$ $[M]^+$ 349.1792, found 349.1790.

***N*,1-Dimethyl-*N*-(4-morpholinobenzyl)-1*H*-indole-3-carboxamide (1e)**; Yield 80%; as a yellow oil; IR (KBr) ν_{max} 3359, 2946, 2833, 1665, 1452, 1115, 1032, 659 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.0 Hz, 1H), 7.18~7.36 (m, 6H), 6.92 (d, J = 8.4 Hz, 2H), 4.72 (s, 2H), 3.87 (t, J = 4.8 Hz, 4H), 3.78 (s, 3H), 3.17 (t, J = 4.8 Hz, 4H), 3.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 163.6, 140.5, 136.9, 136.7, 130.9, 129.0, 126.7, 124.7, 122.6, 121.2, 121.1, 110.1, 109.7, 61.0, 53.5, 49.4, 30.9; HRMS (EI^+) Calcd for $C_{22}H_{25}N_3O_2$ $[M]^+$ 363.1947, found 363.1947.

***N*,1-Dimethyl-*N*-((2-morpholinopyrimidin-5-yl)methyl)-1*H*-indole-3-carboxamide (1f)**; Yield 77%; as a yellow oil; IR (KBr) ν_{max} 3358, 2946, 2833, 1665, 1452, 1116, 1032, 677 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 2H), 7.79 (d, J = 8.0 Hz, 1H), 7.39 (s, 1H), 7.18~7.35 (m, 3H), 4.60 (s, 2H), 3.75~3.85 (m, 11H), 3.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 161.5, 158.0, 136.5, 131.1, 122.6, 121.1, 121.1, 119.1, 110.3, 109.7, 66.8, 44.3, 33.2; HRMS (EI^+) Calcd for $C_{20}H_{23}N_5O_2$ $[M]^+$ 365.1855, found 365.1852.

***N*-(4-(Dimethylamino)benzyl)-*N*-methylbenzamide (3a)**; Yield 97%; as a yellow oil; IR (KBr) ν_{max} 2921, 2801, 1633, 1523, 1399, 1349, 1072, 1011, 836, 755 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47~7.43 (m, 5H), 7.21 (m, 1H), 7.02 (d, J = 7.7 Hz, 1H), 6.65 (dd, J = 18.9, 7.7 Hz, 2H), 4.75 (s, 1H), 4.52 (s, 1H), 3.00 (s, 1.5H), 2.94 (s, 6H), 2.81 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 171.4, 150.1, 136.4, 129.4, 128.4, 127.9, 126.8, 124.7, 123.9, 122.6, 112.6, 54.6, 50.2, 40.5, 36.7, 32.8; HRMS (EI^+) Calcd for $C_{17}H_{20}N_2O$ $[M]^+$ 268.1576, found 268.1577.

***N*-(4-(Dimethylamino)benzyl)-*N*-methyl-4-nitrobenzamide (3b)**; Yield 90%; as a yellow oil; IR (KBr) ν_{max} 3332, 2939, 2865, 2843, 2354, 1648, 1512, 1054, 1033, 1016, 617 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (t, J = 8.8 Hz, 2H), 7.61 (dd, J = 13.2, 8.4 Hz, 2H), 7.25 (d, J = 9.2 Hz, 1H), 6.98 (d, J = 8.0 Hz, 1H), 6.71 (dd, J = 11.6, 8.4 Hz, 2H), 4.66 (s, 1H), 4.34 (s, 1H), 3.06 (s, 1.5H), 2.96 (s, 6H), 2.80 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 169.1, 150.3, 148.2, 142.8, 142.7, 129.6, 127.9, 127.6, 123.9, 122.8, 112.6, 54.5, 50.3, 40.5, 36.4, 33.1; HRMS (EI^+) Calcd for $C_{17}H_{19}N_3O_3$ $[M]^+$ 313.1426, found 313.1426.

4-Bromo-*N*-(4-(dimethylamino)benzyl)-*N*-methylbenzamide (3c); Yield 98%; as a yellow oil; IR (KBr) ν_{max} 2923, 2802, 1685, 1631, 1523, 1446, 1355, 1264, 1064, 844 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51~7.50 (m, 2H), 7.37~7.34 (m, 2H), 7.24~7.22 (m, 1H), 7.00 (d, J = 7.5 Hz, 1H), 6.71~6.69 (m, 2H), 4.63 (s, 1H), 4.38 (s, 1H), 3.03 (s, 1.5H), 2.95 (s, 6H), 2.81 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.2, 150.1, 135.3, 131.6, 129.5, 128.6, 127.7, 124.4, 123.8, 112.8, 54.6, 50.3, 40.5, 36.6, 33.0; HRMS (EI^+) Calcd for $C_{17}H_{19}BrN_2O$ $[M]^+$ 346.0681, found 346.0678.

4-Acetyl-*N*-(4-(dimethylamino)benzyl)-*N*-methylbenzamide (3d); Yield 88%; as a yellow oil; IR (KBr) ν_{max} 2924, 1658, 1633, 1522, 1447, 1315, 1067, 925, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99~7.96 (m, 2H), 7.56 (d, J = 8.2 Hz, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.25 (d, J = 8.4 Hz, 1H), 7.00 (d, J = 8.4 Hz, 1H), 6.73 (d, J = 8.4 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 4.66 (s, 1H), 4.36 (s, 1H), 3.02 (s, 1.5H), 2.93 (s, 6H), 2.80 (s, 1.5H), 2.62 (d, J = 12.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.42, 170.99, 170.28, 150.15, 140.91, 137.56, 129.56, 128.50, 127.79, 127.08, 124.29, 123.30, 112.65, 54.51, 50.19, 40.52, 36.45, 32.85, 26.70; HRMS (EI^+) Calcd for $C_{19}H_{22}N_2O_2$ $[M]^+$ 310.1681, found 310.1682.

4-Benzoyl-*N*-(4-(dimethylamino)benzyl)-*N*-methylbenzamide (3e); Yield 73%; as a yellow oil; IR (KBr) ν_{max} 3730, 3626, 2923, 2354, 1636, 1523, 1351, 1067, 863, 807, 724 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86~7.79 (m, 4H), 7.60~7.47 (m, 5H), 7.27~7.26 (m, 1H), 7.03 (d, J = 8.6 Hz, 1H), 6.74 (d, J = 8.2 Hz, 1H), 6.71(d, J = 8.4 Hz, 1H), 4.68 (s, 1H), 4.41 (s, 1H), 3.04 (s, 1.5H), 2.96 (s, J = 9.0 Hz, 6H), 2.84 (s, 1.5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.08, 171.08, 170.36, 162.24, 150.15, 140.24, 138.33, 137.14, 132.85, 130.15, 129.56, 128.39, 127.81, 126.67, 124.32, 123.35, 122.60, 112.63, 54.58, 50.21, 40.52, 36.64, 32.89; HRMS (EI^+) Calcd for $C_{24}H_{24}N_2O_2$ $[M]^+$ 372.1838, found 372.1837.

***N*-(4-(Dimethylamino)benzyl)-3,4-dimethoxy-*N*-methylbenzamide (3f)**; Yield 88%; as a yellow oil; IR (KBr) ν_{max} 3332, 2940, 2834, 1635, 1510, 1351, 1270, 1233, 1132, 1032, 768, 630 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.22 (br, 1H), 7.05~6.95 (m, 4H), 6.77 (d, J = 8.4 Hz, 2H), 6.98 (d, J = 8.0 Hz, 1H), 6.71 (dd, J = 11.6, 8.4 Hz, 2H), 4.66~4.33 (m, 2H), 3.85 (s, 3H), 3.72 (s, 1.5H), 2.97 (s, 1.5H), 2.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 148.8, 129.4, 128.8, 127.7, 124.5, 120.0, 112.7, 110.8, 110.5, 60.4, 55.9, 40.6, 38.6; HRMS (EI^+) Calcd for $C_{19}H_{24}N_2O_3$ $[M]^+$ 328.1787, found 328.1790.

***N*-(4-(Dimethylamino)benzyl)-*N*-methyl-2-phenylacetamide (3g);** Yield 85%; as a yellow oil; IR (KBr) ν_{max} 3466, 2924, 1645, 1522, 1455, 1398, 1348, 1164, 1105, 946, 809, 727, 697, 571 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.24~7.34 (m, 5H), 7.12 (d, J = 8.4 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 6.68 (t, J = 8.0 Hz, 2H), 4.46 (dd, J = 33.6 Hz, 2H), 3.77 (dd, J = 12.8 Hz, 3H), 2.94 (dd, J = 6.4 Hz, 6H), 2.89 (dd, J = 19.6 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.1, 150.1, 135.3, 129.4, 128.8, 128.6, 127.6, 126.7, 125.1, 123.9, 112.7, 53.2, 50.3, 41.3, 41.0, 40.6, 34.9, 33.7; HRMS (EI^+) Calcd for $C_{18}H_{22}N_2O$ $[M]^+$ 282.1732, found 282.1725.

***N*-(4-(Dimethylamino)benzyl)-*N*-methyldecanamide (3h);** Yield 75%; as a colorless oil; IR (KBr) ν_{max} 3466, 2924, 1652, 1521, 1456, 1399, 1348, 1226, 1163, 947, 802 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.8 Hz, 1H), 6.67~6.72 (m, 2H), 4.46 (dd, J = 23.6 Hz, 2H), 2.94 (d, J = 6 Hz, 6H), 2.89 (dd, J = 9.6 Hz, 3H), 2.31~2.41 (m, 2H), 1.26 (br, 14H), 0.88 (t, J = 4.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.5, 173.1, 150.1, 129.3, 127.4, 125.5, 124.2, 112.7, 52.9, 50.1, 40.6, 34.5, 33.7, 33.5, 33.2, 31.9, 29.4, 25.6, 25.2, 22.7, 14.1; HRMS (EI^+) Calcd for $C_{20}H_{34}N_2O$ $[M]^+$ 318.2671, found 318.2670.

***N*-(4-(Dimethylamino)benzyl)-*N*-methylacetamide (3i);** Yield 80%; as a yellow oil; IR (KBr) ν_{max} 3465, 2926, 1645, 1521, 1404, 1348, 1239, 1118, 809 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, J = 8.4 Hz, 1H), 7.04 (d, J = 8.4 Hz, 1H), 6.68~6.73 (m, 2H), 4.45 (dd, J = 24.8 Hz, 2H), 2.94 (dd, J = 6.0 Hz, 6H), 2.89 (dd, J = 9.2 Hz, 3H), 2.15 (dd, J = 20.8 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.9, 170.5, 150.1, 129.3, 127.5, 125.2, 124.0, 112.7, 53.8, 50.0, 40.6, 35.2, 33.4, 22.0, 21.5; HRMS (EI^+) Calcd for $C_{12}H_{18}N_2O$ $[M]^+$ 206.1419, found 206.1420.

Typical procedure for debenzylation of 4-(alkylamino)benzylamides.

To a solution of debenzylation of 4-(alkylamino)benzylamide (0.093 mmol) in CH_2Cl_2 (1 mL) was added TFA (1 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 8 h and concentrated in vacuum. Then, saturated solution of sodium bicarbonate was slowly added (50 mL) and the reaction mixture extracted with EtOAc (50 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography (CH_2Cl_2 / EtOAc = 90 / 10).

***N*,1-Dimethyl-1*H*-indole-3-carboxamide (2)**; Yield 80%; as a yellow solid; mp 153 °C; IR (KBr) ν_{max} 3425, 2928, 1594, 1525, 1290, 1191, 763 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 7.2 Hz, 1H), 7.65 (s, 1H), 7.18~7.36 (m, 3H), 5.98 (br, 1H), 3.80 (s, 3H), 3.04 (d, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 137.2, 132.2, 125.3, 122.5, 121.4, 120.1, 111.0, 110.1, 33.3, 26.4; HRMS (EI^+) Calcd for $C_{11}H_{12}N_2O$ $[M]^+$ 188.0950, found 188.0950.

Typical procedure for the synthesis of 4-(dimethylamino)benzyl-*N*-methylarylamines.

To a solution of aryl halide (1.26 mmol) in 2-methoxyethanol (5 mL) was added DIPEA (0.45 mL, 2.52 mmol) and *N,N*-dimethyl-4-((methylamino)methyl)aniline (309 mg, 1.89 mmol) at 25 °C in a 10 mL seal tube. The reaction mixture was heated to 80 °C for 8 h. Then, saturated solution of sodium bicarbonate (50 mL) was slowly added and the reaction mixture extracted with EtOAc (50 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography (CH_2Cl_2 / EtOAc = 90 / 10).

***N*-(4-(Dimethylamino)benzyl)-*N*-methyl-5-nitropyridin-2-amine (5a)**; Yield 71%; as a yellow solid; mp 175 °C; IR (KBr) ν_{max} 3442, 3219, 3055, 2864, 1598, 1329, 1291, 1191, 768 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.09 (d, J = 2.8 Hz, 1H), 8.18 (dd, J = 9.6, 2.8 Hz, 1H), 7.11 (d, J = 8.4 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 6.47 (d, J = 9.6 Hz, 1H), 4.80 (s, 2H), 3.16 (s, 3H), 2.29 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 150.2, 146.7, 134.8, 132.8, 128.3, 112.7, 104.3, 53.2, 40.6, 36.5; HRMS (EI^+) Calcd for $C_{15}H_{18}N_4O_2$ $[M]^+$ 286.1426, found 286.1430.

***N*-(4-(Dimethylamino)benzyl)-*N*-methyl-4-nitroaniline (5b)**; Yield 98%; as a yellow solid; mp 171 °C; IR (KBr) ν_{max} 3382, 2940, 2831, 2524, 2354, 2051, 1454, 1310, 1052, 1033, 1018, 618 cm^{-1}; ^1H NMR

(400 MHz, $CDCl_3$) δ 8.09 (d, J = 10.5 Hz, 2H), 7.04 (d, J = 10.5 Hz, 2H), 6.70 (m, 4H), 4.57 (s, 2H), 3.15 (s, 3H), 2.93 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 150.3, 127.7, 126.4, 124.2, 113.1, 111.3, 110.8, 55.8, 40.8, 38.9; HRMS (FAB-MS) Calcd for $C_{16}H_{19}N_3O_2$ $[M]^+$ 285.1476 found 285.1477.

***N*-(4-(Dimethylamino)benzyl)-*N*-methyl-2,4-dinitroaniline (5c)**; Yield 83%; as a yellow solid; mp 169 ^{o}C; IR (KBr) ν_{max} 3357, 2939, 2865, 2843, 2354, 1621, 1454, 1111, 1053, 1053, 1033, 1017, 617 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, J = 2.4 Hz, 1H), 8.16 (dd, J = 2.4, 12.3 1H), 7.11 (m, 3H), 6.79 (m, 2H), 4.51 (s, 2H), 2.95 (s, 3H), 2.90 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.2, 128.3, 128.1, 127.6, 124.1, 121.9, 118.0, 112.7, 57.5, 40.5, 40.4; HRMS (EI^+) Calcd for $C_{16}H_{18}N_4O_4$ $[M]^+$ 330.1330, found 330.1328.

6-((4-(Dimethylamino)benzyl)(methyl)amino)nicotinamide (5d); Yield 68%; as a brown solid; mp 183 ^{o}C; IR (KBr) ν_{max} 2920, 2802, 1631, 1523, 1399, 1349, 1068, 807, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61(dd, J = 2.4, 0.4 Hz, 1H), 7.90 (dd, J = 9.2, 2.4 Hz, 1H), 7.10 (d, J = 8.8 Hz, 2H), 6.69 (dd, J = 6.8, 2.0 Hz, 2H), 6.52 (dd, J = 9.2, 0.4 Hz, 1H), 4.75 (s, 2H), 3.10 (s, 3H), 2.94 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 160.4, 150.0, 148.2, 136.9, 128.1, 125.2, 116.4, 112.7, 52.7, 40.7, 36.1; HRMS (EI^+) Calcd for $C_{16}H_{20}N_4O$ $[M]^+$ 284.1636, found 284.1637.

Methyl 6-((4-(dimethylamino)benzyl)(methyl)amino)nicotinate (5e); Yield 70%; as an ivory solid; mp 90.5 ^{o}C; IR (KBr) ν_{max} 3382, 2947, 2831, 2519, 2354, 2048, 1712, 1603, 1519, 1277, 1118, 1033, 690 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (d, J = 2.4, 1H), 7.97 (dd, J = 8.8, 2.4 Hz, 1H), 7.10 (d, J = 8.8 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 6.48 (d, J = 8.8 Hz, 1H), 4.76 (s, 2H), 3.86 (s, 3H), 3.10 (s, 3H), 2.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 160.8, 151.3, 150.0, 138.2, 128.2, 125.2, 113.7, 112.7, 104.6, 52.7, 51.5, 40.7, 36.1; HRMS (EI^+) Calcd for $C_{17}H_{21}N_3O_2$ $[M]^+$ 299.1632, found 299.1634.

Typical procedure for the synthesis of 4-(dimethylamino)benzyl-*N*-methylaliphaticamines.

To a solution of aliphatic halide (0.285 mmol) in anhydrous THF (1 mL) were added DIPEA (0.119 mL, 0.684 mmol) and 4-(dimethylamino)benzyl-*N*-methylamine (0.342 mmol) at 25 ^{o}C. The reaction mixture was stirred at 25 ^{o}C for 8 h. The reaction mixture was treated with 1*N* NaOH (50 mL) and the product extracted into EtOAc (50 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by amine column chromatography (*n*-hexane/CH_2Cl_2=70/30).

4-((Benzyl(methyl)amino)methyl)-*N*,*N*-dimethylaniline (5f); Yield 80%; as a yellow oil; IR (KBr) ν_{max} 2784, 1614, 1521, 1452, 1345, 1163, 1023, 802, 698 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20~7.36 (m, 7H), 6.71 (d, J = 8.4 Hz, 2H), 3.46 (dd, J = 17.2 Hz, 1H), 2.93 (s, 6H), 2.16 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 149.9, 139.6, 129.9, 129.0, 128.2, 127.1, 126.8, 112.6, 61.5, 42.1, 40.8, 31.6, 22.7, 14.2; HRMS (EI^+) Calcd for $C_{17}H_{22}N_2$ $[M]^+$ 254.1783, found 254.1781.

4-((Decyl(methyl)amino)methyl)-*N*,*N*-dimethylaniline (5g); Yield 80%; as a colorless oil; IR (KBr) ν_{max} 2926, 1743, 1467, 1239, 1042, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, J = 8.4 Hz, 2H), 7.70 (dd, J = 8.4 Hz, 6H), 3.39 (s, 2H), 2.93 (s, 6H), 2.32 (t, J = 7.6 Hz, 2H), 2.16 (s, 3H), 1.50 (t, J = 6.4 Hz, 2H), 1.26 (br, 14H), 0.88 (t, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 149.8, 130.1, 112.5, 61.7, 57.4, 42.1, 40.8, 31.9, 29.7, 29.4, 27.6, 27.4, 22.7, 14.1; HRMS (EI^+) Calcd for $C_{20}H_{36}N_2$ $[M]^+$ 304.2878, found 304.2879.

***N*,*N*-Dimethyl-4-((methyl(phenethyl)amino)methyl)aniline (5h);** Yield 77%; as a colorless oil; IR (KBr) ν_{max} 2943, 2788, 1614, 1521, 1347, 1163, 947, 947, 801, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.14~7.29 (m, 7H), 6.70 (d, J = 8.8 Hz, 2H), 3.48 (s, 2H), 2.93 (s, 6H), 2.80~2.84 (m, 2H), 2.61~2.65 (m, 2H), 2.26 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 149.8, 140.7, 130.128.8, 128.3, 126.7, 125.9, 112.6, 61.6, 59.0, 42.0, 40.8, 33.9; HRMS (EI^+) Calcd for $C_{18}H_{24}N_2$ $[M]^+$ 268,1939, found 268.1938.

Typical procedure for debenzylation of 4-(dimethylamino)benzyl-*N*-methylamide and amine.

To a solution of debenzylation of 4-(dimethylamino)benzyl-*N*-methylamide and amine (0.093 mmol) in MeCN / H_2O(1 mL /1 mL) was added TFA (1 mL) at 25 ^oC in a 10 mL seal tube. The reaction mixture was heated to 80~120 ^oC for 2~5 h and concentrated in vacuum. Then, saturated solution of sodium bicarbonate (50 mL) was slowly added and the reaction mixture extracted with EtOAc (50 mL). The organic layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuum. The residue was purified by column chromatography (CH_2Cl_2 / EtOAc = 50 / 50).

***N*-Methylbenzamide (4a)**; Yield 72%; as a white solid; mp 75.4 ^oC; IR (KBr) ν_{max} 3332, 2940, 2831, 2354, 2643, 1552, 1452, 1412, 1311, 1033, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.77~7.76 (m, 2H), 7.49 (t, J = 7.0 Hz, 1H), 7.43 (t, J = 7.0 Hz, 2H), 6.20 (br, 1H), 3.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.26, 134.64, 131.36, 128.57, 126.81, 26.84; HRMS (EI^+) Calcd for C_8H_9NO $[M]^+$ 135.0684, found 135.0682.

***N*-Methyl-4-nitrobenzamide (4b)**; Yield 80%; as a yellow solid; mp 207 ^oC; IR (KBr) ν_{max} 3382, 2968, 2865, 2354, 1695, 1611, 1055, 1033, 1016 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.30 (dd, J = 9.2, 2.0 Hz, 2H), 7.93 (dd, J = 7.2, 2.0 Hz, 2H), 6.18 (br, 1H), 3.07 (d, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 166.1, 149.6, 140.2, 128.0, 123.9, 29.7, 27.1; HRMS (EI^+) Calcd for $C_8H_8N_2O_3$ $[M]^+$ 180.0535, found 180.0534.

4-Bromo-*N*-methylbenzamide (4c); Yield 72%; as a white solid; mp 150 ^oC; IR (KBr) ν_{max} 3343, 2940, 2831, 2519, 2354, 2049, 1642, 1554, 1484, 1032, 839, 750, 623 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, J = 8.6 Hz, 2H), 7.56 (d, J = 8.6 Hz, 2H), 6.16 (br, 1H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.24, 133.43, 131.80, 128.46, 126.03, 26.91; HRMS (EI^+) Calcd for C_8H_8BrNO $[M]^+$ 212.9789, found 212.9787.

4-Acetyl-*N*-methylbenzamide (4d); Yield 75%; as a white solid; mp 128 °C; IR (KBr) ν_{max} 3383, 2939, 2831, 2354, 1731, 1683, 1648, 1413, 1267, 1032, 857, 614 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.6 Hz, 2H), 7.85 (d, J = 8.6 Hz, 2H), 6.28 (br, 1H), 3.04 (d, J = 4.9 Hz, 3H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.47, 167.22, 139.10, 138.51, 128.55, 127.17, 26.97, 26.82; HRMS (EI^+) Calcd for $C_{10}H_{11}NO_2$ $[M]^+$ 177.0790, found 177.0788.

4-Benzoyl-*N*-methylbenzamide (4e); Yield 70%; as a white solid; mp 127 °C; IR (KBr) ν_{max} 3382, 2939, 2831, 1650, 1453, 1278, 1033, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 13.4, 8.5 Hz, 4H), 7.80 (d, J = 7.1 Hz, 2H), 7.62 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 6.20 (br, 1H), 3.06 (d, J = 4.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.98, 167.33, 140.02, 137.88, 137.05, 132.88, 130.18, 130.09, 128.46, 126.82, 27.00; HRMS (EI^+) Calcd for $C_{15}H_{13}NO_2$ $[M]^+$ 239.0946, found 239.0947.

3,4-Dimethoxy-*N*-methylbenzamide (4f); Yield 75%; as a yellow solid; mp 127 °C; IR (KBr) ν_{max} 3381, 2947, 2831, 1649, 1454, 1052, 1033, 617 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 2.0 Hz, 1H), 7.26 (dd, J = 8.4, 2.0 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.11 (br, 1H), 3.93 (s, 3H), 3.92 (s, 3H), 3.01 (d, J = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 151.6, 149.0, 127.4, 119.1, 110.6, 110.3, 56.0, 26.9; HRMS (EI^+) Calcd for $C_{10}H_{13}NO_3$ $[M]^+$ 195.0895, found 195.0896.

***N*-Methyl-2-phenylacetamide (4g);** Yield 88%; as a yellow oil; IR (KBr) ν_{max} 3306, 1652, 1558, 1413, 1205, 1133, 724, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25~7.38 (m, 5H), 5.36 (br, 1H), 3.58 (s, 2H), 2.76 (d, J = 4.8, 7.7 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.7, 134.9, 129.6, 129.1, 127.4, 43.8, 26.5; HRMS (EI^+) Calcd for $C_9H_{11}NO$ $[M]^+$ 149.0841, found 149.0798.

***N*-Methyldecanamide (4h);** Yield 76%; as a yellow oil; IR (KBr) ν_{max} 3299, 2919, 1634, 1566, 1465, 1205, 1163, 722, 597 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.41 (br, 1H), 2.81(d, J = 4.8 Hz, 3H), 2.16 (t, J = 7.6 Hz, 2H), 1.27 (br, 14H), 0.88 (t, J = 6.4 Hz, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.8, 36.8, 31.9, 29.4, 25.8, 22.7, 14.1; HRMS (EI^+) Calcd for $C_{11}H_{23}NO$ $[M]^+$ 185.1780, found 185.1786.

N-Methylacetamide (4i); Yield 65%; as a yellow oil; IR (KBr) ν_{max} 3305, 1645, 1567, 1415, 1162, 600 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.15 (br, 1H), 2.79 (d, J = 4.8 Hz, 3H), 1.98 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.0, 26.4, 23.0; HRMS (EI^+) Calcd for C_3H_7NO $[M]^+$ 73.0528, found 73.0336.

***N*-Methyl-5-nitropyridin-2-amine (6a)**; Yield 75%; as a yellow solid; mp 180 °C; IR (KBr) ν_{max} 3561, 3493, 1633, 1570, 1333, 1205, 842 cm^{-1}; ^1H NMR (400 MHz, DMSO) δ 8.91 (s, 1H), 8.08 (br, 2H), 6.54 (d, J = 9.2 Hz, 1H), 2.89 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 161.9, 146.9, 134.1, 131.5, 108.5, 27.8; HRMS (EI^+) Calcd for $C_6H_7N_3O_2$ $[M]^+$ 153.0540, found 153.0538.

***N*-Methyl-4-nitroaniline (6b)**; Yield 91%; as a yellow solid; mp 168 °C; IR (KBr) ν_{max} 3373, 2939, 2831, 2354, 1745, 1455, 1306, 1111, 1052, 1033, 618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (m, 2H), 6.54 (m, 2H), 4.55 (br, 1H), 2.94 (d, J = 5.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 154.3, 138.4, 126.6, 110.9, 29.9; HRMS (FAB-MS) Calcd for $C_7H_8N_2O_2$ $[M]^+$ 152.0587, found 152.0586.

***N*-Methyl-2,4-dinitroaniline (6c)**; Yield 67%; as a yellow solid; mp 173 °C; IR (KBr) ν_{max} 3355, 2940, 2831, 1740, 1454, 1368, 1216, 1051, 1033, 618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.16 (d, J = 2.66 Hz, 1H), 8.58 (br, 1H), 8.32 (m, 1H), 6.93 (d, J = 9.52, 1H), 3.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.1, 136.2, 130.5, 124.3, 113.5, 30.3; HRMS (EI^+) Calcd for $C_7H_7N_3O_4$ $[M]^+$ 197.0436, found 197.0437.

6-(Methylamino)nicotinamide (6d); Yield 71%; as a white solid; mp 164 °C; IR (KBr) ν_{max} 3382, 2941, 2831, 1740, 1668, 1616, 1375, 1206, 1120, 1052, 1033, 1018, 617 cm^{-1}; ^1H NMR (400 MHz, DMSO) δ 8.53 (d, J = 2 Hz, 1H), 7.87 (dd, J = 8.8, 2.4 Hz, 1H), 6.51 (d, J = 8.8 Hz, 1H), 2.91 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 171.1, 162.7, 149.7, 137.6, 118.3, 108.5, 28.6; HRMS (EI^+) Calcd for $C_7H_9N_3O$ $[M]^+$ 151.0746, found 151.0744.

Methyl 6-(methylamino)nicotinate (6e); Yield 80%; as a white solid; mp 92 °C; IR (KBr) ν_{max} 3382, 2948, 2864, 2831, 1713, 1614, 1537, 1434, 1284, 1053, 1033, 1017, 779, 618 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 2 Hz, 1H), 8.01 (dd, J = 8.8, 2.4 Hz, 1H), 6.36 (d, J = 8.8 Hz, 1H), 5.06 (br, 1H), 3.87 (s, 3H), 2.99 (d, J = 2 Hz, 3H); ^{13}C NMR (100 MHz, DMSO) δ 166.5, 161.6, 151.6, 138.6, 115.1, 104.9, 51.7, 29.0; HRMS (EI^+) Calcd for $C_8H_{10}N_2O_2$ $[M]^+$ 166.0743, found 166.0742.

***N*-Methyl-1-phenylmethanamine (6f);** Yield 70%; as a yellow oil; IR (KBr) ν_{max} 3320, 2932, 1645, 1521, 1454, 1353, 739, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 3.73 (s, 2H), 2.44 (s, 3H), 1.42 (br, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.2, 128.4, 128.2, 127.0, 55.1, 36.1; HRMS (EI^+) Calcd for $C_8H_{11}N$ $[M]^+$ 121.0891, found 121.0899.

***N*-Methyldecan-1-amine (6g);** Yield 82%; as a yellow oil; IR (KBr) ν_{max} 2926, 1744, 1467, 1239, 1041, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.62 (br, 2H), 2.47 (s, 3H), 1.58~1.63 (m, 5H), 1.27 (br, 6H), 0.86~0.89 (m, 8H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 31.9, 29.5, 29.3, 28.6, 27.2, 25.9, 22.7; HRMS (EI^+) Calcd for $C_{11}H_{25}N$ $[M]^+$ 171.1987, found 171.1980.

***N*-Methyl-2-phenylethan-1-amine (6h);** Yield 75%; as a colorless oil; IR (KBr) ν_{max} 3314, 2938, 1549, 1455, 1384, 1306, 1110, 748, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31~7.20 (m, 5H), 2.85~2.76 (m, 4H), 2.43 (s, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 140.1, 128.7, 128.4, 161.1, 53.3, 36.4, 36.3; HRMS (EI^+) Calcd for $C_9H_{13}N$ $[M]^+$ 135.1048, found 135.1039.

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