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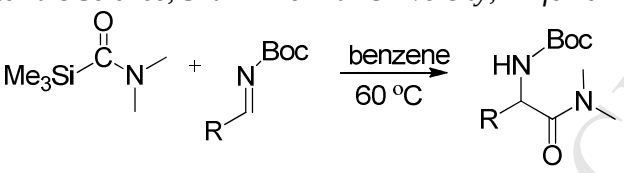

1 **2** **3**

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Efficient synthesis of *α*-(*N*-Boc)aminoamides by addition of a carbamoylsilane to *N*-Boc-imines

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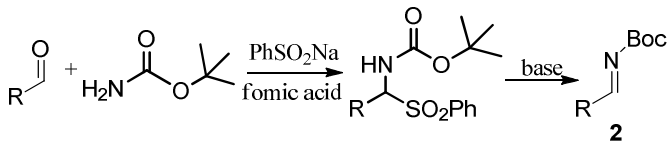
ABSTRACT

N,*N*-Dimethylcarbamoyl(trimethyl)silane reacted with *N*-Boc-imines in anhydrous benzene under catalysts-free conditions to afford *N*-Boc-protected *α*-amino amides in good yields (72–89%). The electronic property and the steric hindrance of substituent on the *N*-Boc-imines affected the reaction.

1. Introduction

α-Amino amides have been investigated extensively, as they are a common structural feature in a wide range of natural products and pharmaceutical agents, and are the basic subunit of peptides and proteins.[1] They have also been used as building blocks for the synthesis of different heterocycles, and ligands for the metal-catalysts.[2] Commonly, the Ugi reaction has been used to provide *α*-amino amides,[3] whose various limitations are under continual improvement.[4] Recently, Mita et al. have shown that the copper-catalyzed silylation of *N*-benzenesulfonyl imines, then carboxylation under a CO_2 atmosphere can afford *α*-amino acids.[5] Reeves et al. reported that the addition of the carbamoyl anion to *N*-sulfinylimines can also afford *α*-amino amides.[6] However, these methods limited by the restricted availability of isocyanides, the difficulty of deacylating the protected amino function, the unstable of lithium reagents, the high pressure of carbon dioxide, low reaction temperature and harsh reaction conditions. We have recently found that carbamoylsilanes add to the C=N bond of sulfonylimines to afford *α*-(*N*-sulfonyl)amino amides.[7] However, the desulfonation of *α*-(*N*-sulfonyl)amino amides require metal Na or Li,[8] which influence other groups in pharmaceutical synthesis. So the search for a simple and practical method remains a challenge. We now found that the addition of *N*,*N*-dimethylcarbamoyl(trimethyl)silane to many types of easily obtainable *N*-Boc-imines could offer good yields of Boc-protected *α*-amino amides derivatives, which can be deprotected under mildly acidic conditions to form *α*-amino amides. To the best of our knowledge, carbamoylsilane has never been reported for the synthesis of Boc-protected *α*-amino amides, we report here on the successful attempt in this regard.

2. Results and discussion



Scheme 1 The preparation of *N*-Boc-imines **2**

N-Boc-imines **2** were easily prepared by the reaction of aldehydes, *tert*-butyl carbamate and sodium benzene sulfinic acid in a mixture solution of methanol, formic acid and water, followed by removing benzene sulfinic acid in basic solution (Scheme 1),[9, 10] which were allowed to react with 1.1 equiv of *N*, *N*-dimethylcarbamoyl(trimethyl)silane **1**[11] under anhydrous conditions, good yields of *N*-Boc-protected *α*-amino amides **3** were obtained, generally within a matter of hours at 60 □ (Table 2).

Table 1 Solvent effect on the addition of *N*,*N*-dimethylcarbamoyl(trimethyl)silane to benzaldehyde *N*-Boc imine

Entry	Solvent	Temp (℃)	Time[a] (h)	Yield[b,c] (%)
1	dichloromethane	35	46	0
2	acetonitrile	75	33	58
3	THF	60	28	64
4	toluene	60	26	67
5	benzene	60	22	74

[a]To complete consumption of carbamoylsilane. [b]Isolated yield based on benzaldehyde *N*-Boc imine. [c]1:1.2 mol ratio of benzaldehyde *N*-Boc imine

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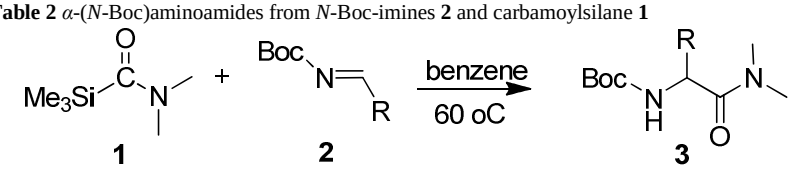
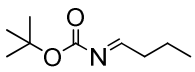
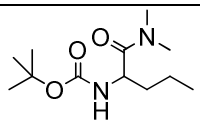
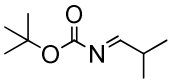
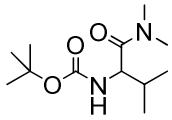
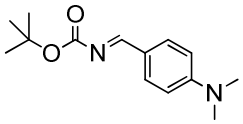
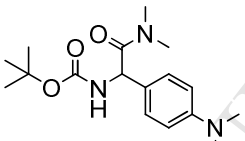
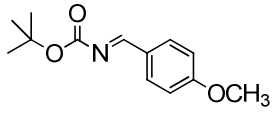
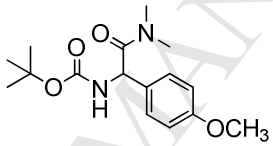
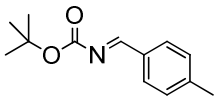
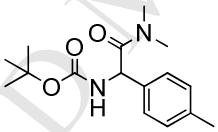
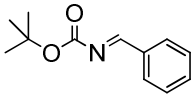
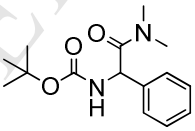
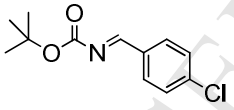
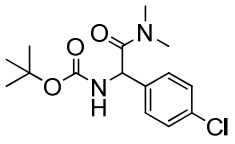
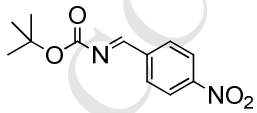
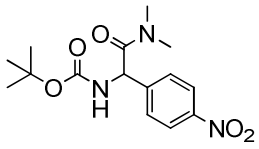
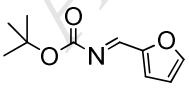
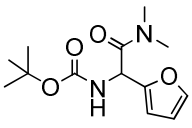
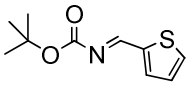
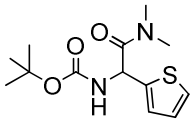
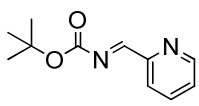
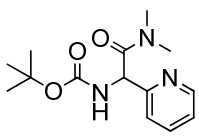
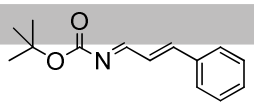
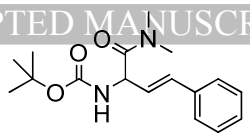
and carbamoylsilane.

Initial examination was focused on the investigation of the solvent effect in the reaction. The addition of *N*,*N*-dimethyl-carbamoyl(trimethyl)silane to benzaldehyde *N*-Boc imine was chosen as a model reaction. The reaction proceeded smoothly in all tested solvents except dichloromethane (no product). When the reaction was conducted in benzene, the product was obtained in high yield and the reaction time was short. Several other solvents, including toluene, acetonitrile and THF, gave inferior results compared to benzene (Table 1).

Table 2 *α*-(*N*-Boc)aminoamides from *N*-Boc-imines **2** and carbamoylsilane **1**

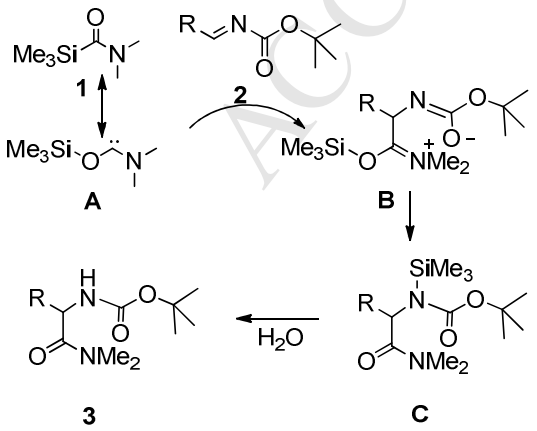


Entry	*N*-Boc-imines	Product	Time[a] (h)	Yield [b,c] (%)
1	**2a** 	**3a** 	17	89
2	**2b** 	**3b** 	23	86
3	**2c** 	**3c** 	20	76
4	**2d** 	**3d** 	20	77
5	**2e** 	**3e** 	24	72
6	**2f** 	**3f** 	22	74
7	**2g** 	**3g** 	19	89
8	**2h** 	**3h** 	17	84
9	**2i** 	**3i** 	19	76
10	**2j** 	**3j** 	21	73
11	**2k** 	**3k** 	18	82

12	**2l**		16	78	
		3l 			

[a] To complete consumption of carbamoylsilane **1** in benzene at 60 ℃
[b] Isolated yield based on *N*-Boc-imines.
[c] 1:1.1 mol ratio of *N*-Boc-imines and carbamoylsilane.

Next, to explore the scope of the reaction between different *N*-Boc-imines and carbamoylsilane **1** under optimal conditions to furnish the *N*-Boc-protected *α*-amino amides, we tested the representative *N*-Boc-imines bearing aliphatic group, aryl or heteroaryl on the C=N bond. Experimental results were summarized in Table 2. For the *N*-Boc-imines derived from different aldehydes, all of the reactions gave good yields. A comparison of the results obtained from **2a**, **2b** indicates that the steric environment is an important factor in the addition reaction since longer reaction time was needed and lower yield of product was achieved in case of **2b** than in case of **2a**. The data of Table 2 (entries 3-11) indicates that the addition reaction is sensitive to electronic factors. Aromatic aldehyde *N*-Boc imines possessing an electron-donating group on the aromatic ring, such as the dimethylamino, methoxy or methyl group, gave slightly lower yields (entries 3-5). In contrast, substitution of an electron-withdrawing group on the aromatic ring, such as a nitro or chloro, led to higher yields (entries 7 and 8). Benzaldehyde *N*-Boc imine **2f** afforded the addition product in moderate yield (entry 6). *N*-Boc-imines **2i** and **2j** containing an electron-rich heteroaryl group, the furyl and thienyl, reacted with carbamoylsilane **1** to afford good yields of desired addition products **3i** and **3j** (entries 9 and 10). Reaction rate was faster compared to benzaldehyde *N*-Boc imine **2f**. *N*-Boc-imine **2k** possessing an electron-deficient heteroaryl (pyridyl) gave the addition product in high yield (entry 11). We conclude that, in general, aromatic aldehyde *N*-Boc imines possessing an electron-withdrawing group (or electron-deficient heteroaryl aldehyde *N*-Boc imines) gave a better yield than those having an electron-donating group (or electron-rich heteroaryl aldehyde *N*-Boc imines). An electron-withdrawing substituent on the *N*-Boc-imines accelerates the reaction and leads to an improved yield. In addition, the cinnamic aldehyde *N*-Boc imine **2l** has proved more reactive toward reaction of **1** than all of aromatic aldehyde *N*-Boc imines, since the reaction proceeded with faster rate in case of **2l** than in case of **2c-h**, and compound **3l** corresponding to 1,2-addition product was exclusively obtained in good yield. This result further confirms steric hindrance play an important role in addition reaction.



Scheme 2 Proposed reaction mechanism

A possible route to addition products **3** is presented in Scheme 2. Carbamoylsilane **1** can rearrange to its nucleophilic carbene form **A**,[12] which attacked the *N*-Boc-imines to produce an unstable intermediate **B**, followed by silyl group 1,4-migration to give the adducts **C**. The latter can be hydrolyzed in the separation process to form *α*-(*N*-Boc)amino amides **3**.

3. Conclusions

In conclusion, a novel and highly efficient procedure has been developed for the preparation of a series of *N*-Boc-protected *α*-amino amides by the addition of *N*,*N*-dimethylcarbamoyl-(trimethyl)silane to *N*-Boc-imines. In all cases, good yields of the products were obtained under mild reaction conditions. This approach is simple and mild procedure, no catalysts conditions, less byproducts and good yields for the preparation of various *α*-amino amides. We anticipate that our study may draw significant attention of chemists working on the development of synthetic methodologies and will find applications in organic and medicinal chemistry. Further investigations to develop an asymmetric version of this reaction are now in progress.

4. Experimental section

4.1 General

All reactions were carried out using standard Schlenk techniques unless specified other otherwise. Dry benzene was freshly distilled from sodium and benzophenone as a moisture indicator under Ar atmosphere before use. All liquid aldehydes were freshly distilled under reduced pressure. ^{1}H (600 MHz) and ^{13}C (150.8 MHz) NMR spectra were recorded on Bruker (AV600) NMR spectrometer. All spectra were recorded at room temperature in deuterated chloroform ($CDCl_3$) δ=7.28 ppm for proton NMR, δ=77.00 ppm for carbon NMR) unless otherwise stated using tetramethylsilane (TMS) as an internal standard. Chemical shifts are expressed in parts per million (ppm) and coupling constants in Hertz (Hz). Infrared spectra were recorded as potassium bromide (KBr) discs for solids or thin films on sodium chloride plates for oils on an IMPACT-410 spectrophotometer. Elemental analysis was performed on an EA-1108 analyzer. Melting points were measured with a STUART SMP 10 melting point apparatus and uncorrected. The monitoring of reaction and checking of purity of the product were done using pre-coated silica gel plates (Merck 60 PF_{254}). Column chromatography was performed using Merck silica gel 200. Visualization was achieved by UV (254 nm) light detection and iodine staining.

4.2 General procedure for Boc-sulfonyl carbamates [9,10]

To a 50 mL round bottom flask charged with a stir bar was added *tert*-butyl carbamate (1 g, 8.55 mmol), sodium benzenesulfinic acid (2.8 g, 17.09 mmol), methanol (8.5 mL), water (17 mL), aldehyde (8.55mmol) and formic acid (98%, 8.55 mmol) sequentially. The reaction mixture was stirred at 23 ℃ for 48 h. The reaction mixture was filtered and the precipitate was washed with water and diethyl ether to yield clean Boc-sulfonyl carbamates.

4.3 General procedure for the preparation of *N*-Boc-imines 2f, 2h, 2k and 2l[9,10]

To a 25 mL round bottom flask containing a stirring solution of Boc-sulfonyl carbamate (1.0 mmol) in dichloromethane (16 mL) was added aqueous K_2CO_3 (16 mL, 1.4 mol • L^{-1}), the resulting biphasic mixture was vigorously stirred at 23℃ for 5 h. The organic layer was separated and the aquoaus layer was extracted with dichloromethane (2×20 mL). The combined organics were dried over $MgSO_4$ and concentrated in *vacuo* at room temperature to yield the desired *N*-Boc-imines.

*4.3.1. Benzaldehyde N-Boc imine (**2f**).*[10a, 13] Colourless oil; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.90 (s, 1H, C<u>H</u>=N), 7.95–7.93 (m, 2H, Ar–<u>H</u>), 7.60–7.28 (m, 3H, Ar–<u>H</u>), 1.61 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 168.2, 163.1, 134.9, 132.9, 130.0, 128.8, 81.2, 27.9.

*4.3.2. (4-Nitro)benzaldehyde N-Boc imine (**2h**).*[10c, 16] White solid, mp=101.0–103.0 ℃; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.89 (s, 1H, C<u>H</u>=N), 8.34 (d, 2H, *J* = 8.4 Hz, Ar–<u>H</u>), 8.10 (d, 2H, *J* = 8.4 Hz, Ar–<u>H</u>), 1.62 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 166.2, 161.7, 150.5, 139.3, 130.6, 124.0, 83.2, 27.9.

*4.3.3. 2-Pyridinecarboxaldimine (**2k**).* Yellow solid, mp=145.0–147.0 ℃; IR (KBr) ν_{max}: 3424, 2980, 1715, 1494, 1244, 1149, 1011, 774 cm^{-1}; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 9.97 (1H, s, C<u>H</u>=N), 8.61 (d, 1H, *J* = 4.2 Hz, pyridyl-6-<u>H</u>), 7.74 (t, 1H, *J* = 7.8 Hz, pyridyl-4-<u>H</u>), 7.57 (d, 1H, *J* = 8.4 Hz, pyridyl-3-<u>H</u>), 7.22–7.20 (m, 1H, pyridyl-5-<u>H</u>), 1.27 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 156.1, 153.9, 147.6, 136.3, 123.2, 121.8, 80.0, 28.0. Anal. Calcd for $C_{11}H_{14}N_2O_2$: C ,64.06; H, 6.84; N, 13.58. Found: C, 64.23; H, 6.62; N, 13.76.

*4.3.4. Cinnamicaldehyde N-Boc imine (**2l**).*[9,17] Pale yellow oil; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.70 (d, 1H, *J* = 9.2 Hz, C<u>H</u>=N), 7.54 (d, 2H, *J* = 3.7 Hz, Ar–<u>H</u>), 7.42-7.38 (m, 3H, Ar–<u>H</u>), 7.36 (d, 1H, *J* = 15.9 Hz, =C<u>H</u>), 6.99 (dd, 1H, *J* = 9.2, 15.9 Hz, =C<u>H</u>=), 1.57 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 171.6, 162.3, 150.5, 134.7, 130.8, 129.0, 128.1, 126.8, 81.9, 27.9.

4.4 General procedure for the preparation of *N*-Boc-imines 2a-e, 2g, 2i and 2j[9,10]

To a 25 mL round bottom flask containing a stirring solution of Boc-sulfonyl carbamate (1.0 mmol) in dichloromethane (13.3 mL) was added dry Cs_2CO_3 (3.26 g, 7.5 mmol). The mixture was vigorously stirred at 23 ℃ for 1 h. The slurry was filtered and the organic phase was concentrated in *vacuo* at 23 ℃ to yield the desired *N*-Boc-imines.

*4.4.1. Butylaldehyde N-Boc imine (**2a**).*[18] Colourless oil; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.27 (s, 1H, C<u>H</u>=N), 1.64 (t, 2H, *J* = 7.2 Hz, C<u>H</u>$_2$C=), 1.52 (s, 9H, (C<u>H</u>$_3$)$_3$C), 1.46–1.43 (m, 2H, C<u>H</u>$_2$), 0.98 (t, 3H, *J* = 7.2 Hz, C<u>H</u>$_3$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 175.4, 162.1, 82.0, 38.1, 27.8, 18.3, 13.7.

*4.4.2. iso-Butylaldehyde N-Boc imine (**2b**).*[18] Colourless oil; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.14 (s, 1H, C<u>H</u>=N), 2.55–2.51 (m, 1H, C<u>H</u>), 1.50 (s, 9H, (C<u>H</u>$_3$)$_3$C), 1.09, 1.02 (dd, 6H, *J* = 5.4 Hz, (C<u>H</u>$_3$)$_2$CH); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 178.8, 162.4, 82.0, 34.4, 27.8, 18.1.

*4.4.3. (4-Dimethylamino)benzaldehyde N-Boc imine (**2c**).* Yellow solid, mp=99.0–101.0 ℃; IR (KBr) ν_{max}: 3340, 2980, 1683, 1583, 1535, 1366, 1240, 1144, 990, 826 cm^{-1}; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.94 (s, 1H, C<u>H</u>=N), 7.84 (d, 2H, *J* = 8.4 Hz, Ar–<u>H</u>), 6.70 (d, 2H, *J* = 8.4 Hz, Ar–<u>H</u>), 3.10 (s, 6H, (C<u>H</u>$_3$)$_2$N), 1.60 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 171.1, 163.4, 154.2, 133.0, 121.6, 111.3, 81.1, 40.0, 28.0; Anal. calcd for $C_{14}H_{20}N_2O_2$: C, 67.71; H, 8.12; N, 11.28. Found: C, 67.91; H, 8.36; N, 11.08.

*4.4.4. (4-Methoxy)benzaldehyde N-Boc imine (**2d**).*[10a, 13] ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.91 (s, 1H, C<u>H</u>=N), 7.91 (d, 2H, *J* = 7.8 Hz, Ar–<u>H</u>), 6.99 (d, 2H, *J* = 7.8 Hz, Ar–<u>H</u>), 3.90 (s, 3H, C<u>H</u>$_3$), 1.60 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 168.3, 163.3, 160.1, 132.2, 128.5, 114.4, 80.7, 54.7, 28.0.

*4.4.5. (4-Methyl)benzaldehyde N-Boc imine (**2e**).*[10a, 13] Colourless oil; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.85 (s, 1H, C<u>H</u>=N), 7.67 (d, 2H, *J* = 7.8 Hz, Ar–<u>H</u>), 6.85 (d, 2H, *J* = 7.8 Hz, Ar–<u>H</u>), 2.42 (s, 3H, C<u>H</u>$_3$), 1.59 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 168.4, 163.3, 143.7, 132.5, 130.2, 129.7, 81.0, 28.0, 21.4.

*4.4.6. (4-Chloro)benzaldehyde N-Boc imine (**2g**).*[10a, 16] ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.86 (s, 1H, C<u>H</u>=N), 7.88 (d, 2H, *J* = 8.4 Hz, Ar–<u>H</u>), 7.47 (d, 2H, *J* = 8.4 Hz, Ar–<u>H</u>), 1.61 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 168.2, 162.3, 139.8, 132.5, 131.3, 129.3, 82.5, 27.9.

*4.4.7. 2-Furaldehyde N-Boc imine (**2i**).*[10b, 14] Pale yellow oil; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 8.79 (s, 1H, C<u>H</u>=N), 7.70 (s, 1H, Furyl-5-<u>H</u>), 7.25 (d, 1H, *J* = 3.0 Hz, Furyl-3-<u>H</u>), 6.62–6.59 (dd, 1H, *J* = 3.0, 1.7 Hz, Furyl-4-<u>H</u>), 1.58 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 162.3, 157.6, 150.9, 148.2, 121.5, 113.2, 82.6, 28.0.

*4.4.8. 2-Thenylaldehyde N-Boc imine (**2j**).*[10b, 15] Pale yellow oil; ^{1}H NMR (600 MHz, $CDCl_3$) δ_H: 9.10 (s, 1H, C<u>H</u>=N), 7.69 (d, 1H, *J* = 3.6 Hz, Thienyl-3-<u>H</u>), 7.68 (d, 1H, *J* = 1.8 Hz, Thienyl-5-<u>H</u>), 7.20–7.19 (m, 1H, Thienyl-4-<u>H</u>), 1.59 (s, 9H, (C<u>H</u>$_3$)$_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 163.6, 162.2, 140.2, 137.1, 134.2, 128.4, 82.2, 27.9.

4.5 General procedure for the synthesis of *α*-(*N*-Boc) amino-*N',N'*-dimethyl amides 3

A Schlenk tube fitted with a Teflon vacuum stopcock and micro stirbar was flame heated under vacuum and refilled with Ar. *N*-Boc-imines **2** (0.50 mmol) and anhydrous benzene (2 mL) were added at ice bath temperature. After 20 min, carbamoylsilane **1** (0.55 mmol) was added. The sealed reaction mixture was stirred at 60 ℃ until no carbamoylsilane **1** could be detected by TLC. Volatiles were removed in *vacuo* to afford the crude product which was purified by column chromatography on silica gel (petroleum ether/ethyl acetate combination) to give *N*-Boc-protected *α*-amino amides **3**.

*4.5.1. α-(N-Boc)amino-N',N'-dimethyl pentanamide (**3a**).* Yield= 89%; mp=63.5–65.0 ℃; IR (KBr) ν_{max}: 3254, 1711, 1638, 1550, 1279, 1175, 1118 cm^{-1}; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 5.38 (d, 1H, *J* = 8.4 Hz, N<u>H</u>), 4.62 (q, 1H, *J* = 8.4, 5.4 Hz, C<u>H</u>N), 3.09, 3.08 (ss, 3H, C<u>H</u>$_3$N), 2.98, 2.97 (ss, 3H, C<u>H</u>$_3$N), 1.43–1.64 (m, 13H, (C<u>H</u>$_3$)$_3$C, C<u>H</u>$_2$C<u>H</u>$_2$), 0.95 (t, 3H, *J* = 7.2, C<u>H</u>$_3$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 172.5, 155.6, 79.4, 49.9, 37.1, 35.7, 35.6, 28.4, 18.6, 13.9; Anal. Calcd for $C_{12}H_{24}N_2O_3$: C, 58.99; H, 9.90; N, 11.47. Found: C, 58.76; H, 10.15; N, 11.23.

*4.5.2. α-(N-Boc)amino-N',N'-dimethyl-iso-pentanamide (**3b**).* Yield=86%; mp=81.5–83.0 ℃; IR (KBr) ν_{max}: 3318, 1711, 1638, 1539, 1397, 1252, 1175 cm^{-1}; ^{1}H NMR (600MHz, $CDCl_3$) δ_H: 5.32 (d, 1H, *J* = 9.0, N<u>H</u>), 4.49 (q, 1H, *J* = 9.0, 6.0 Hz, C<u>H</u>N), 3.11 (s, 3H, C<u>H</u>$_3$N), 2.98, (s, 3H, C<u>H</u>$_3$N), 1.93–1.97 (m, 1H, C<u>H</u>(CH$_3$)$_2$), 1.45 (s, 9H, (C<u>H</u>$_3$)$_3$C), 0.98 (d, 3H, *J* = 7.2, C<u>H</u>$_3$CH), 0.91 (d, 3H, *J* = 7.2, C<u>H</u>$_3$CH); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 172.2, 155.9, 79.4, 54.9, 37.4, 35.6, 31.6, 28.4, 19.5, 17.3; Anal. Calcd for $C_{12}H_{24}N_2O_3$: C, 58.99; H, 9.90; N, 11.47. Found: C, 58.79; H, 9.67; N, 11.68.

*4.5.3. α-(N-Boc)amino-N',N'-dimethyl-(4-dimethylamino)phenylacetamide (**3c**).* Yield=76%; mp=148.5–150.0 □; IR (KBr) ν_{max}: 3291, 1706, 1654, 1524, 1366, 1248, 1165 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 6.67–7.24 (m, 4H, Ar–H), 5.94 (d, 1H, *J* = 7.8 Hz, NH), 5.47 (d, 1H, *J* = 7.8 Hz, CHN), 2.90–2.97 (m, 12H, $(CH_3)_2$NPh, $(CH_3)_2$N), 1.41 (s, 9H, $(CH_3)_3$C); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 170.6, 155.1, 150.2, 128.6, 125.5, 112.6, 79.3, 54.6, 40.4, 36.9, 35.9, 28.4; Anal. Calcd for $C_{17}H_{27}N_3O_3$: C, 63.53; H, 8.47; N, 13.07. Found: C, 63.81; H, 8.69; N, 12.89.

*4.5.4. α-(N-Boc)amino-N',N'-dimethyl-(4-methoxy)phenylacetamide (**3d**).* Yield=77%; mp=138.0–139.5 □; IR (KBr) ν_{max}: 3302, 1703, 1641, 1510, 1263, 1162 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 6.87–7.32 (m, 4H, Ar–H), 6.01(d, 1H, *J* = 7.2 Hz, NH), 5.51 (d, 1H, *J* = 7.2 Hz, CHN), 3.81 (s, 3H, CH_3O), 2.99 (s, 3H, CH_3N), 2.09 (s, 3H, CH_3N), 1.42 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 170.3, 159.4, 155.1, 130.1, 129.0, 114.3, 79.6, 55.3, 54.6, 36.9, 36.0, 28.4; Anal. Calcd for $C_{16}H_{24}N_2O_4$: C, 62.32; H, 7.84; N, 9.08. Found: C, 62.56; H, 7.56; N, 9.29.

*4.5.5. α-(N-Boc)amino-N',N'-dimethyl-(4-methyl)phenylacetamide (**3e**).* Yield=72%; mp=133.0–134.5 □; IR (KBr) ν_{max}: 3296, 1703, 1641, 1523, 1392, 1263, 1162 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 7.16–7.28 (m, 4H, Ar–H), 6.20 (d, 1H, *J* = 7.2 Hz, NH), 5.30 (d, 1H, *J* = 7.2 Hz, CHN), 3.00 (s, 3H, CH_3N), 2.90 (s, 3H, CH_3N), 2.35 (d, 3H, *J* = 2.4 Hz, CH_3), 1.42 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 170.2, 155.1, 137.9, 135.0, 130.0, 127.6, 79.6, 54.9, 36.9, 36.0, 28.4, 21.2; Anal. Calcd for $C_{16}H_{24}N_2O_3$: C, 65.73; H, 8.27; N, 9.58. Found: C, 65.90; H, 8.56; N, 9.79.

*4.5.6. α-(N-Boc)amino-N',N'-dimethylphenylacetamide (**3f**).* Yield=74%; mp=121.5–123.0 □; IR (KBr) ν_{max}: 3410, 1706, 1638, 1485, 1397, 1164 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 7.30–7.40 (m, 5H, Ar–H), 6.05 (d, 1H, *J* = 7.8 Hz, NH), 5.57 (d, 1H, *J* = 7.8 Hz, CHN), 2.99 (s, 3H, CH_3N), 2.91 (s, 3H, CH_3N), 1.42 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 170.1, 155.1, 138.0, 129.0, 128.2, 127.9, 127.7, 79.7, 55.2, 36.9, 36.0, 28.4; Anal. Calcd for $C_{15}H_{22}N_2O_3$: C, 64.73; H, 7.97; N, 10.06. Found: C, 64.51; H, 7.74; N, 10.16.

*4.5.7. α-(N-Boc)amino-N',N'-dimethyl-(4-chloro)phenylacetamide (**3g**).* Yield=89%; mp=137.5–139.0 □; IR (KBr) ν_{max}: 3287, 1695, 1638, 1535, 1396, 1164 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 7.33–7.36 (m, 4H, Ar–H), 6.09 (d, 1H, *J* = 7.2 Hz, NH), 5.53 (d, 1H, *J* = 7.2 Hz, CHN), 3.00 (s, 3H, CH_3N), 2.91 (s, 3H, CH_3N), 1.42 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 169.2, 155.0, 136.6, 134.1, 129.2, 79.9, 54.5, 36.9, 36.0, 28.4; Anal. Calcd for $C_{15}H_{21}ClN_2O_3$: C, 57.60; H, 6.77; N, 8.96. Found: C, 57.80; H, 6.68; N, 8.73.

*4.5.8. α-(N-Boc)amino-N',N'-dimethyl-(4-nitro)phenylacetamide (**3h**).* Yield=84%; mp=174.5–176.0 □; IR (KBr) ν_{max}: 3291, 1706, 1654, 1524, 1366, 1165 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 8.23 (d, 2H, *J* = 7.8 Hz, Ar–H), 7.60 (d, 2H, *J* = 7.8 Hz, Ar–H), 6.21 (d, 1H, *J* = 7.2 Hz, NH), 5.65 (d, 1H, *J* = 7.2 Hz, CHN), 3.02 (s, 3H, CH_3N), 2.94 (s, 3H, CH_3N), 1.42 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 168.8, 154.9, 147.7, 145.1, 128.8, 124.3, 80.2, 54.5, 37.0, 36.1, 28.3; Anal. Calcd for $C_{15}H_{21}N_3O_5$: C, 55.72; H, 6.55; N, 13.00. Found: C, 55.62; H, 6.32; N, 13.21.

*4.5.9. α-(N-Boc)amino-N',N'-dimethyl-(2)-furylacetamide (**3i**).* Yield=76%; mp=89.0–90.5 □; IR (KBr) ν_{max}: 3384, 1706, 1643, 1489, 1405, 1169 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 7.37, (d, 1H, *J* = 10.2 Hz, Furyl-5-H), 6.30–6.34 (m, 2H, Furyl-3-H, Furyl-4-H), 5.95 (s, 1H, NH), 5.71–5.74 (m, 1H, CHN), 3.02 (s, 3H, CH_3N), 3.00 (s, 3H, CH_3N), 1.45, 1.44 (ss, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 168.0, 155.1, 150.6, 142.6, 110.5, 107.9, 80.0, 49.2, 36.9, 36.9, 28.4; Anal. Calcd for $C_{13}H_{20}N_2O_4$: C, 58.19; H, 7.51; N, 10.44. Found: C, 58.45; H, 7.73; N, 10.21.

*4.5.10. α-(N-Boc)amino-N',N'-dimethyl-(2)-thienylacetamide (**3j**).* Yield=73%; mp=73.5–74.5 □; IR (KBr) ν_{max}: 3409, 3314, 1703, 1645, 1523, 1482, 1167 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 7.26 (d, 1H, *J* = 4.8 Hz, Thienyl-5-H), 6.94–7.01 (m, 2H, Thienyl-3-H, Thienyl-4-H), 5.99 (d, 1H, *J* = 7.8 Hz, NH), 5.83 (d, 1H, *J* = 7.8 Hz, CHN), 3.01 (s, 3H, CH_3N), 2.99 (s, 3H, CH_3N), 1.43 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 169.3, 154.9, 140.5, 126.8, 126.0, 125.9, 79.9, 50.2, 37.1, 36.0, 28.4; Anal. Calcd for $C_{13}H_{20}N_2O_3S$: C, 54.91; H, 7.09; N, 9.85. Found: C, 54.68; H, 7.31; N, 9.62.

*4.5.11. α-(N-Boc)amino-N',N'-dimethyl-(2)-pyridylacetamide (**3k**).* Yield=82%; yellow liquid; IR (KBr) ν_{max}: 3414, 3387, 1710, 1653, 1485, 1390, 1247, 1164 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 8.55 (d, 1H, *J* = 4.2 Hz, pyridyl-6-H), 7.68-7.71 (m, 1H, pyridyl-4-H), 7.46 (d, 1H, *J* = 7.8 Hz, pyridyl-3-H), 7.20–7.22 (m, 1H, pyridyl-5-H), 6.25 (d, 1H, *J* = 7.2 Hz, NH), 5.80 (d, 1H, *J* = 7.2 Hz, CHN), 3.11 (s, 3H, CH_3N), 3.01 (s, 3H, CH_3N), 1.44 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 169.5, 158.0, 155.2, 149.4, 137.1, 122.8, 121.8, 79.8, 56.6, 37.4, 36.1, 28.4; Anal. Calcd for $C_{14}H_{21}N_3O_3$: C, 60.20; H, 7.58; N, 15.04. Found: C, 60.46; H, 7.79; N, 15.33.

4.5.12. α-(N-Boc)amino-N',N'-dimethyl-4-phenyl-2-butenylamide *(**3l**).* Yield=78%; yellow liquid; IR (KBr) ν_{max}: 3417, 3387, 1710, 1649, 1489, 1396, 1256, 1168 cm^{-1}; ^1H NMR (600MHz, $CDCl_3$) δ_H: 7.27–7.40 (m, 5H, Ar–H), 6.65 (d, 1H, *J* = 16.2 Hz, Ar-CH=), 6.15 (q, 1H, *J* = 16.2, 7.2 Hz, =CH-CHN), 5.82 (d, 1H, *J* = 7.8 Hz, NH), 5.23 (t, 1H, *J* = 7.8, 7.2 Hz, CHN), 3.11 (s, 3H, CH_3N), 3.03 (s, 3H, CH_3N), 1.46 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (151MHz, $CDCl_3$) δ_C: 169.9, 155.0, 136.1, 133.3, 128.6, 128.1, 126.7, 124.5, 79.7, 53.5, 53.0, 37.0, 36.0, 28.4; Anal. Calcd for $C_{17}H_{24}N_2O_3$: C, 67.08; H, 7.95; N, 9.20. Found: C, 67.26; H, 7.74; N, 9.30.

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