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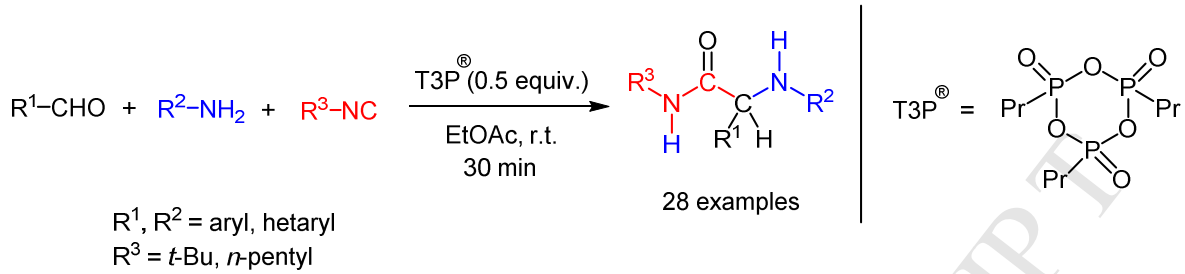
Graphical abstract



Study on the propylphosphonic anhydride (T3P®) mediated Ugi-type three-component reaction. Efficient synthesis of an α-amino amide library

Mátyás Milen,* András Dancsó, Tamás Földesi, Balázs Volk

Egis Pharmaceuticals Plc., Directorate of Drug Substance Development, P. O. Box 100, H-1475 Budapest, Hungary

*To whom correspondence should be addressed. Phone: +36 1 8035874, e-mail: milen.matyas@egis.hu

Abstract

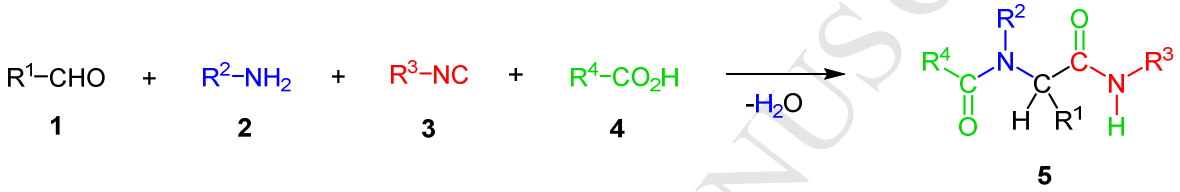
In the present work, a mild and simple synthesis of α-amino amides has been developed via the one-pot three-component ABC type Ugi reaction of a wide variety of aromatic aldehydes and primary aromatic amines, and two different aliphatic isocyanides. The reactions took place rapidly at room temperature in the presence of 1-propanephosphonic acid cyclic anhydride (T3P®), rendering possible the highly efficient preparation of an α-amino amide library in medium to excellent yields. This study represents the first case in which T3P® has been used in the Ugi reaction.

Key words

Multicomponent reaction, Three-component Ugi reaction, α-Amino amides, T3P®, Mechanism

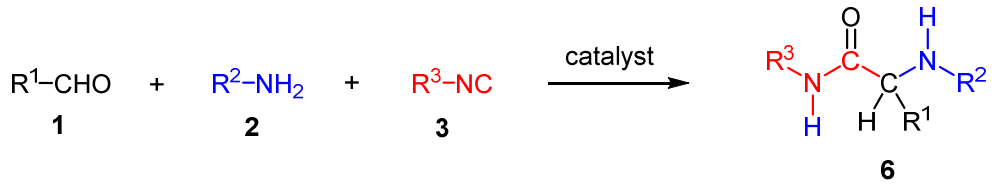
INTRODUCTION

Multicomponent reactions (MCRs) play an important role in organic and medicinal chemistry as a tool to generate small-molecule libraries.[1] One of the most important MCRs is the Ugi four-component reaction (Ugi-4CR) involving a carbonyl compound (**1**), an amine (**2**), an isocyanide (**3**), and a carboxylic acid (**4**) to form an α-aminoacyl amides (**5**) and water as the only by-product (Scheme 1).[2–3] Hitherto, several modifications of the classical Ugi reaction have been discovered and applied in the synthesis of amino acids, peptides, heterocycles, drug substances, natural products and polymers.[4–10]



Scheme 1. Ugi four-component reaction

Moreover, various three-component Ugi reactions (Ugi-3CR) have been described in the literature.[11–14] The catalytic Ugi-3CR (ABC type, which means that one equivalent of each reactant is used) of an aldehyde (**1**), a primary amine (**2**), and an isocyanide (**3**) resulting in α-aminoamides **6** was first published by List and Pan in 2008 (Scheme 2).[15] The condensation of benzaldehyde, *p*-anisidine, and *tert*-butyl isocyanide was investigated in detail. It was found that the reactions (toluene, 80 °C, 24 h) did not take place in the presence of *p*-toluenesulfonic acid (*p*TsOH), diphenylphosphine oxide [$Ph_2P(O)H$] or without catalysts. When using other acids, such as phenylboronic acid [$PhB(OH)_2$], diphenyl phosphate [$(PhO)_2P(O)(OH)$], scandium triflate [$Sc(OTf)_3$], phenylphosphonic acid [$PhP(O)(OH)_2$], and diphenylphosphinic acid [$Ph_2P(O)(OH)$], the appropriate α-amino amide (**6**, R^1 = Ph; R^2 = 4-MeO-C_6H_4; R^3 = *t*-Bu) was obtained only in poor yields (8–35%). However, an excellent result was achieved when applying phenylphosphinic acid [PhP(O)(OH)H] as the catalyst. In this case, the corresponding α-amino amide was prepared in 91% yield. This reaction was extended to various amines, aldehydes, and isocyanides. The products were usually obtained in good yields (Method A, Scheme 2).



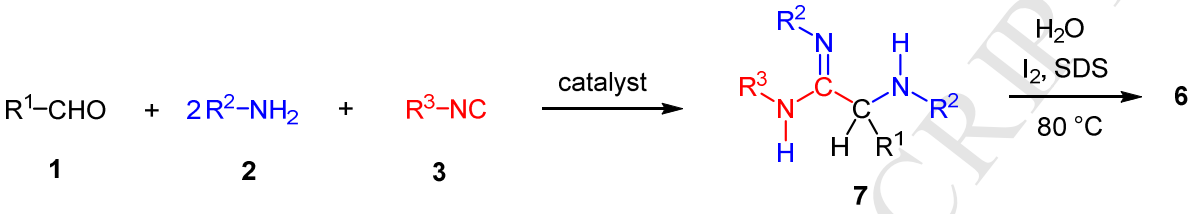
Method A: PhP(O)(OH)H, toluene, 80 °C, 12−36 h, 25 examples, 36−91% yields (ref. 5)
Method B: $ZnCl_2$, MeOH, rt, 12 h, 7 examples, 83−93% yields (ref. 6)
Method C: CSA, EtOH, rt, 48 h, 18 examples, 55−75% yields (ref. 7)
Method D: $B(OH)_3$, H_2O, rt, 45−60 min, 15 examples, 75−90% yields (ref. 8)
Method E: *p*TSIA, MeOH, rt, 12−24 h, 25 examples, 52−71% yields (ref. 9)

Scheme 2. Catalytic three-component ABC type Ugi reaction

Shaabani et al. studied Lewis acid-catalyzed Ugi-3CR of aldehydes, 2-aminophenol derivatives, and cyclohexyl isocyanide.[16] According to their observation, the reaction proceeded smoothly in the presence of $ZnCl_2$ in methanol at room temperature. The desired products (**6**, R^1 = Ph, substituted phenyl, Bu; R^2 = 2-HO-C_6H_4, 2-HO-4-Me-C_6H_3, 3-HO-pyrid-2-yl; R^3 = *c*-Hex) were obtained in good yields. However, the scope of the reaction was not studied extensively, only seven representatives were synthesized (Method B, Scheme 2). The same research group applied successfully cellulose sulphuric acid (CSA), a biodegradable biopolymer catalyst inter alia in the synthesis of α-amino amides (**6**, R^1 = Ph, substituted phenyl; R^2 = Ph, Bn, allyl; R^3 = *c*-Hex, *t*-Bu, *p*-$TsSO_2CH_2$) via Ugi-3CR.[17] Compounds **6** were prepared in good yields under mild conditions in ethanol but this protocol required a prolonged (48 h) reaction time (Method C, Scheme 2).

In 2013, Kumar and his group described a green synthetic approach for the preparation of 2-arylamino-2-phenylacetamide derivatives (**6**, R^1 = phenyl, substituted phenyl; R^2 = phenyl, substituted phenyl; R^3 = cyclohexyl or *tert*-butyl) using the reagents in aqueous medium. This reaction was catalyzed by boric acid [$B(OH)_3$] and the desired products were obtained in good to excellent yields (Method D, Scheme 2).[18] In the same year, Li and co-workers reported an Ugi-3CR mediated by *p*-toluenesulfinic acid (*p*TSIA, Method E, Scheme 2).[19] In this case α-amino amidines (**7**, see Scheme 3) were also produced beside α-amino amides (**6**, R^1 = Ph, substituted phenyl, *i*-Bu, benzofuran-2-yl; R^2 = substituted phenyl; R^3 = alkyl, substituted phenyl). Furthermore, when amines were used in excess (more than 1.5 equiv.), compounds **7** were afforded as the main products. Synthesis of α-amino amidines (**7**) via AB^2C type (B^2 means that

two equivalents of amine were used in this case) Ugi-3CR is known in the literature and it can also be catalysed by ZnO-nanoparticles[20] or molecular iodine[21] (Scheme 3). It is also noteworthy to mention that neutral hydrolysis of compounds **7** in the presence of I_2 and sodium dodecyl sulfate (SDS) led to α-amino amides (**6**, R^1 = Ph, substituted phenyl, pyridine-4-yl; R^2 = Ph, substituted phenyl; R^3 = *t*-Bu, *c*-Hex, *p*-Ts-CH_2).[20]



Scheme 3. Synthesis of α-amino amidines (**7**) and α-amino amides (**6**) via catalytic three-component AB^2C type Ugi reaction

Recently, propylphosphonic anhydride (T3P®) has attracted tremendous attention in synthetic organic chemistry. The T3P® reagent has several advantages including easy storability, low toxicity, broad functional group tolerance and easy work-up procedures due the formation of water-soluble by-products. A number of applications have been described using this reagent, for example in organic functional group transformations, rearrangements, multicomponent reactions, carbon-carbon bond formations, moreover in the synthesis of various heterocycles and natural products.[22–31]

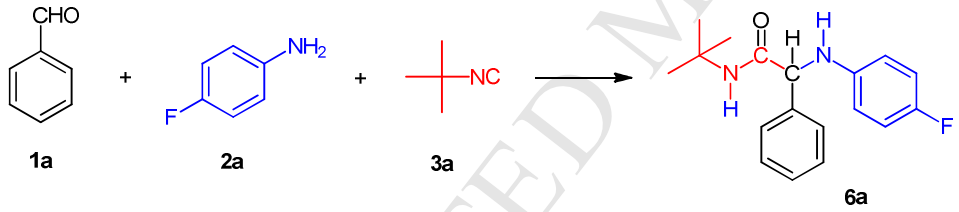
Herein, we would like to report the synthesis of α-amino amides (**6**) via T3P®-assisted Ugi-3CR of aromatic aldehydes (**1**), primary aromatic amines (**2**), and aliphatic isocyanides (**3**) providing the desired compounds (**6**) with good yields. To the best of our knowledge, this is the first case that T3P® is used in an Ugi reaction.

RESULTS AND DISCUSSION

To optimize the T3P®-mediated Ugi-3CR, we extensively tested experimental parameters. Initially, benzaldehyde (**1a**), 4-fluoroaniline (**2a**), and *tert*-butyl isocyanide (**3a**) (1 equiv. of each) were chosen as starting materials (Table 1) and the reaction was investigated with various amounts of T3P® reagent. When using 1.0 equiv. of T3P® in EtOAc at room temperature, the desired α-amino amide **6a** was obtained in 58% yield (Table 1, entry 1). When the amount of

T3P® was increased to 1.5 or reduced to 0.2 equiv., compound **6a** was afforded in similar yields (60−61%) after 24 h (entries 2–4). A further decrease of T3P® amount to 0.02 equiv. proved to be disadvantageous (entry 5). It is worth mentioning that under the same reaction conditions without T3P®, no formation of expected product **6a** occurred (entry 6). This result confirms previous observations that Ugi-3CR does not take place in the absence of catalyst.[15] Another investigation was conducted aiming at the reaction time and temperature screen. It was found that the reaction time could be decreased to 30 min at room temperature and the optimal amount of T3P® was 0.5 equiv. (entries 7–9). Higher temperature both in EtOAc and DMF solvents has not made a positive effect on the reaction (entries 10, 11). A crude reaction mixture (entry 8) was analysed by GC-MS/LC-MS, and the appropriate Schiff base (8–10%), α-amino amidine (3–4%) and other unidentified by-products could be detected beside the main product **6a**. Although the presence of the Schiff base intermediate might indicate an incomplete conversion, a longer reaction time (entry 3) or an increased amount of isocyanide **3a** did not lead to higher yields of **6a**.

Table 1. Screening of reaction conditions for the construction of α-amino amides



1a + **2a** + **3a** → **6a**

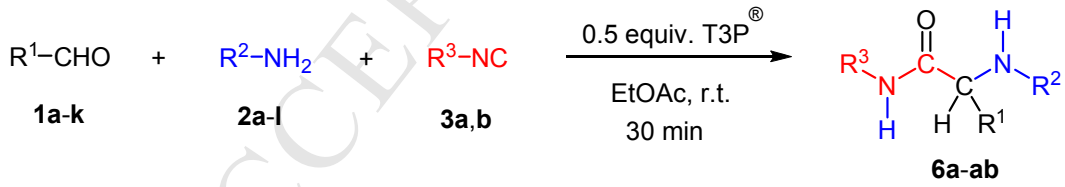
Entry	T3P® (equiv.)	Temperature	Reaction time (h)	Yield[a] (%)
1	1.0	r. t.	24	58
2	1.5	r. t.	24	61
3	0.5	r. t.	24	61
4	0.2	r. t.	24	60
5	0.02	r. t.	24	19
6	-	r. t.	24	0
7	1.0	r. t.	0.5	58
8	0.5	r. t.	0.5	58
9	0.2	r. t.	0.5	24
10	0.5	reflux	0.5	46

11[b]	0.5	80 °C	0.5	43

[a] Yield of the isolated product.

[b] The reaction was carried out in DMF and a DMF solution of T3P® reagent was used.

After establishing optimal reaction conditions, we surveyed the scope and limitations of the T3P®-assisted Ugi-3CR (Scheme 4). Initially, the reaction of benzaldehyde (**1a**) with various primary aromatic amines (**2a**–**l**) and *tert*-butyl isocyanide (**3a**) was examined (Table 2, entries 1–12). The products from amines were usually obtained in good yields. However, when 2-(methylthio)aniline (**2c**) and 2,4-dimethylaniline (**2j**) were used as the starting materials, the appropriate α-amino amides (**6c**, **j**) were isolated only in 33 and 46% yields, respectively (entries 3, 10). Heteroaromatic 5-aminoquinoline (**2l**) can be employed in this synthesis with poor yield (entry 12). Next, the reaction was investigated with a variety of aromatic aldehydes (**1b**–**k**), aniline (**2b**), and *tert*-butyl isocyanide (**3a**) (entries 13–22). Both substituted benzaldehydes (**1b**–**f**) and other aromatic ones, such as 2-naphthaldehyde (**1g**) and 9*H*-fluorene-2-carbaldehyde (**1h**) were applied successfully affording the products in over 65% yield. The reaction also works with heteroaromatic carbaldehydes (**1i**–**k**), the corresponding α-amino amides (**6t**–**w**) were obtained in 53–85% yields. Finally, the reaction was extended using 1-pentyl isocyanide (**3b**) instead of *tert*-butyl isocyanide (**3a**) and four representatives (**6y**–**ab**) were prepared in variable yields (entries 25–28). Under these reaction conditions, use of non-aromatic amines, such as cyclopropylamine and benzylamine (with benzaldehyde and *tert*-butyl isocyanide) or that of an aliphatic aldehyde, butyraldehyde (with aniline and *tert*-butyl isocyanide) did not provide the desired products.



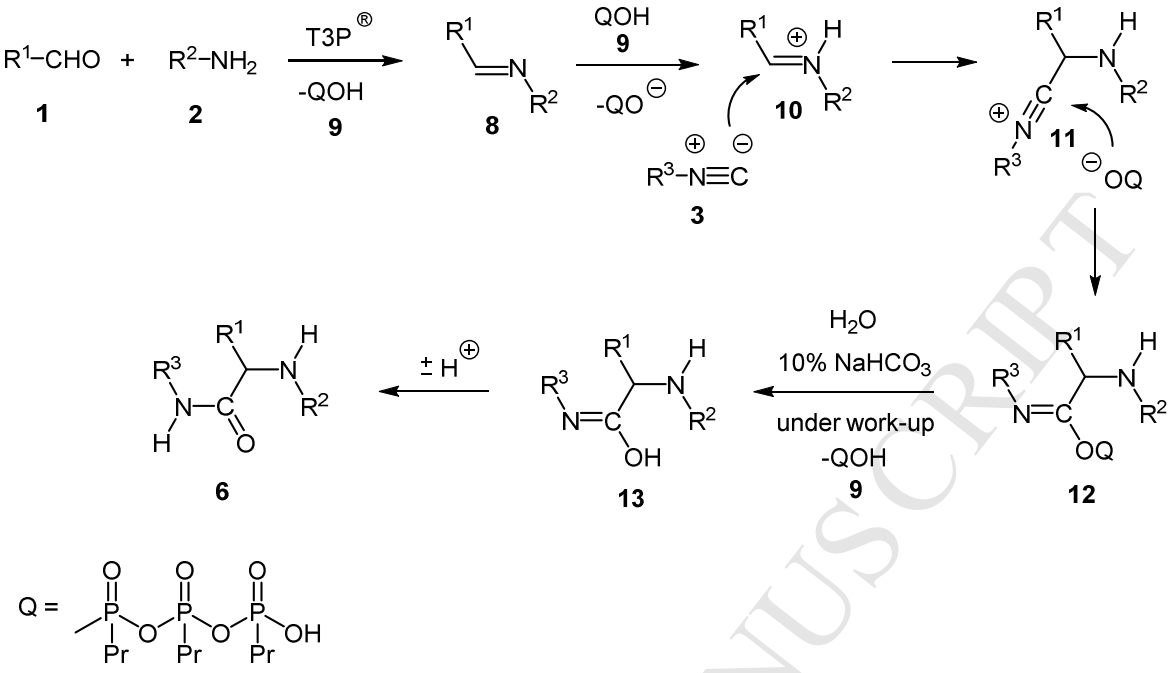
Scheme 4. T3P®-promoted three-component ABC type Ugi reaction

Table 2. Yields of the reactions resulting in α-amino amides **6a−ab**

Entry	R^1	R^2	R^3	Product	Yield (%)
1	Ph (**1a**)	4-FC_6H_4 (**2a**)	*t*-Bu (**3a**)	**6a**	58
2	Ph (**1a**)	Ph (**2b**)	*t*-Bu (**3a**)	**6b**	77
3	Ph (**1a**)	2-$MeSC_6H_4$ (**2c**)	*t*-Bu (**3a**)	**6c**	33
4	Ph (**1a**)	3-ClC_6H_4 (**2d**)	*t*-Bu (**3a**)	**6d**	70
5	Ph (**1a**)	3-$F_3CC_6H_4$ (**2e**)	*t*-Bu (**3a**)	**6e**	63
6	Ph (**1a**)	3-$PhOC_6H_4$ (**2f**)	*t*-Bu (**3a**)	**6f**	57
7	Ph (**1a**)	4-$F_3CC_6H_4$ (**2g**)	*t*-Bu (**3a**)	**6g**	56
8	Ph (**1a**)	4-NCC_6H_4 (**2h**)	*t*-Bu (**3a**)	**6h**	90
9	Ph (**1a**)	4-PhC_6H_4 (**2i**)	*t*-Bu (**3a**)	**6i**	79
10	Ph (**1a**)	2,4-$Me_2C_6H_3$ (**2j**)	*t*-Bu (**3a**)	**6j**	46
11	Ph (**1a**)	2,3-dihydro-1*H*-inden-5-yl (**2k**)	*t*-Bu (**3a**)	**6k**	63
12	Ph (**1a**)	quinolin-5-yl (**2l**)	*t*-Bu (**3a**)	**6l**	35
13	3-FC_6H_4 (**1b**)	Ph (**2b**)	*t*-Bu (**3a**)	**6m**	72
14	3-$F_3CC_6H_4$ (**1c**)	Ph (**2b**)	*t*-Bu (**3a**)	**6n**	69
15	3-$PhOC_6H_4$ (**1d**)	Ph (**2b**)	*t*-Bu (**3a**)	**6o**	79
16	4-$F_3CC_6H_4$ (**1e**)	Ph (**2b**)	*t*-Bu (**3a**)	**6p**	70
17	4-PhC_6H_4 (**1f**)	Ph (**2b**)	*t*-Bu (**3a**)	**6q**	75
18	naphthalen-2-yl (**1g**)	Ph (**2b**)	*t*-Bu (**3a**)	**6r**	89
19	9*H*-fluoren-2-yl (**1h**)	Ph (**2b**)	*t*-Bu (**3a**)	**6s**	67
20	furan-2-yl (**1i**)	Ph (**2b**)	*t*-Bu (**3a**)	**6t**	53
21	pyridin-3-yl (**1j**)	Ph (**2b**)	*t*-Bu (**3a**)	**6u**	85
22	quinolin-4-yl (**1k**)	Ph (**2b**)	*t*-Bu (**3a**)	**6v**	68
23	4-$F_3CC_6H_4$ (**1e**)	4-PhC_6H_4 (**2i**)	*t*-Bu (**3a**)	**6w**	66
24	4-PhC_6H_4 (**1f**)	4-NCC_6H_4 (**2h**)	*t*-Bu (**3a**)	**6x**	79
25	Ph (**1a**)	Ph (**2b**)	*n*-pentyl (**3b**)	**6y**	89
26	Ph (**1a**)	4-FC_6H_4 (**2a**)	*n*-pentyl (**3b**)	**6z**	47
27	Ph (**1a**)	4-NCC_6H_4 (**2h**)	*n*-pentyl (**3b**)	**6aa**	63
28	naphthalen-2-yl (**1l**)	Ph (**2b**)	*n*-pentyl (**3b**)	**6ab**	89

The structures of synthesized compounds (**6a**–**ab**) were characterized by IR, ^{1}H NMR, ^{13}C NMR spectroscopy, and HRMS. Products **6b**,[18] **6d**,[15] and **6g**[15] have been described previously, while compounds **6a**,**c**,**e**,**f**,**h**–**ab** are new.

A plausible mechanism for the formation of α-amino amides (**6**) via Ugi-3CR in the presence of T3P® is outlined in Scheme 5. The first step is the T3P®-promoted condensation of the aldehyde (**1**) and the amine (**2**) to form an imine (**8**) along with 1,5-dihydroxy-1,3,5-tripropyltriphosphoxane 1,3,5-trioxide (QOH, **9**). In the next step, Schiff base **8** is protonated by QOH (**9**) and the iminium ion (**10**) obtained reacts with isocyanide **3** in a nucleophilic addition to provide the nitrilium ion (**11**). Subsequently, another nucleophilic addition takes place at intermediate **11** with the QO^- anion to generate phosphonic acid ester **12**. Finally, hydrolysis of **12** followed by tautomerization of imidic acid **13** leads to the final product, α-amino amide (**6**). In order to exclude the possibility of the incomplete hydrolysis of **12** during work-up and subsequent loss of yield, the relative rate of the hydrolysis has been determined based on the following experiments using benzaldehyde (**1a**), 4-fluoroaniline (**2a**) and *tert*-butyl isocyanide (**3a**). Two further batches of **6a** were prepared using the optimal conditions determined previously, but after the addition of **3a** and a 30 min stirring at room temperature, 1.0 and 2.5 equivalents of water were added, and the reaction mixtures were stirred for further 24 h. After the regular work-up procedure, we have not found significant differences among these yields and the yield of the original experiment. Accordingly, the hydrolysis of **12a** to **13a** is sufficiently fast to be completed during the usual work-up procedure.



Scheme 5. Proposed mechanism for the T3P®-mediated three-component Ugi reaction

CONCLUSIONS

In conclusion, we have developed a simple and convenient method for the preparation of α-amino amides using a T3P®-promoted three-component Ugi reaction starting from an aromatic aldehyde, a primary aromatic amine and an aliphatic isocyanide. The advantages of this procedure are the short reaction time, good yields, mild conditions, and high variability of the reagents.

EXPERIMENTAL SECTION

General

All melting points were determined on a Büchi B-540 capillary melting point apparatus and are uncorrected. IR spectra were obtained on a Bruker Vector 22 FT spectrometer in KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were recorded at 303 K on a Bruker Avance III HD (600 and 150 MHz for ^{1}H and ^{13}C NMR spectra, respectively) or a Bruker Avance III (400 and 100 MHz for ^{1}H and ^{13}C NMR spectra, respectively) spectrometer. $CDCl_3$ was used as the solvent and tetramethylsilane (TMS) as the internal standard. Chemical shifts (δ) and coupling constants (J)

are given in ppm and in Hz, respectively. Mass spectra were recorded on a Bruker O-TOF MAXIS Impact mass spectrometer coupled to a Dionex Ultimate 3000 RS HPLC system with a diode array detector. The reactions were followed by analytical thin layer chromatography on silica gel 60 F_{254} and LC–MS chromatography. Purifications by flash chromatography were carried out using Merck 107736 silica gel 60 H using a hexane-ethyl acetate solvent system. All reagents were purchased from commercial sources. Analytical samples of new compounds were obtained by recrystallization from the solvents or solvent mixtures given below in parentheses.

General procedure for the synthesis of α-amino amides (6a–ab). The appropriate aromatic aldehyde (**1a**−**k**, 1.0 mmol) and primary aromatic amine (**2a**−**l**, 1.0 mmol) were dissolved in EtOAc (5 mL), and T3P® (Aldrich 50% solution in EtOAc, 0.3 mL, 0.5 mmol) was added. After 5 min, *tert*-butyl isocyanide (**3a**, 1.0 mmol) or 1-pentyl isocyanide (**3b**, 1.0 mmol) was added and the mixture was stirred at room temperature for 30 min. Then the mixture was diluted with EtOAc (10 mL) and washed with a 10% aqueous $NaHCO_3$ solution (10 mL). The organic layer was dried (Na_2SO_4), filtered and evaporated. The residue was purified by flash column chromatography to afford products **6a**–**ab**.

***N-tert*-Butyl-2-[(4-fluorophenyl)amino]-2-phenylacetamide (6a).** Yield: 174 mg (58%); white crystals; mp 141–142 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.36. IR (KBr, cm^{-1}): 3402, 3283, 1649, 1562, 1510, 1223, 818, 699. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43–7.40 (m, 2H), 7.39–7.37 (m, 2H), 7.35–7.32 (m, 1H), 6.90–6.87 (m, 2H), 6.57–6.56 (m, 1H), 6.55–6.54 (m, 1H), 6.43 (br s, 1H), 4.54 (br d, J = 1.1 Hz, 1H), 4.47 (br s, 1H), 1.31 (s, 9H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.0, 156.6 (d, J = 236.8 Hz), 143.0 (d, J = 2.0 Hz), 139.1, 129.2, 128.5, 127.2, 115.7 (d, J = 22.5 Hz), 114.7 (d, J = 7.6 Hz), 65.2, 51.2, 28.5 ppm. HRMS calcd. for $C_{18}H_{22}FN_2O$ $[M+H]^+$ 301.1716; found 301.1712.

***N-tert*-Butyl-2-phenyl-2-(phenylamino)acetamide (6b).**[18] Yield: 218 mg (77%); white crystals; mp 132–133 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.37. IR (KBr, cm^{-1}): 3409, 3280, 1650, 1602, 1558, 1509, 759. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.41 (m, 2H), 7.40–7.36 (m, 2H), 7.35–7.31 (m, 1H), 7.21–7.17 (m, 2H), 6.81–6.78 (m, 1H), 6.64–6.63 (m, 1H), 6.62–6.61 (m, 1H), 6.52 (br s, 1H), 4.60 (d, J = 2.2 Hz, 1H), 4.49 (br s, 1H). 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 146.8, 139.3, 129.2 (two signals), 128.4, 127.3, 119.0, 113.9, 64.9, 51.2, 28.5 ppm. HRMS calcd. for $C_{18}H_{23}N_2O$ $[M+H]^+$ 283.1810; found 283.1804.

***N-tert*-Butyl-2-{[2-(methylsulfanyl)phenyl]amino}-2-phenylacetamide (6c).** Yield: 109 mg (33%); white crystals; mp 146–147 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.42. IR (KBr, cm^{-1}): 3320, 1651, 1559, 1493, 733. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.46–7.43 (m, 2H), 7.42–7.41 (m, 1H), 7.40–7.38 (m, 2H), 7.36–7.34 (m, 1H), 7.17–7.13 (m, 1H), 6.78–6.74 (m, 1H), 6.55 (d, J = 8.0 Hz, 1H), 6.38 (br s, 1H), 5.75 (br d, J = 1.7 Hz, 1H), 4.64 (br d, J = 2.8 Hz, 1H), 2.35 (s, 3H), 1.31 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 146.7, 139.1, 133.3, 129.2, 129.1, 128.4, 127.1, 121.5, 118.9, 111.7, 64.7, 51.2, 28.5, 18.2 ppm. HRMS calcd. for $C_{19}H_{25}N_2OS$ $[M+H]^+$ 329.1688; found 329.1687.

***N-tert*-Butyl-2-[(3-chlorophenyl)amino]-2-phenylacetamide (6d).**[15] Yield: 233 mg (70%); white crystals; mp 128–129 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.42. IR (KBr, cm^{-1}): 3418, 3343, 1652, 1597, 1542, 1492, 1223, 989, 732. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.40 (m, 2H), 7.39–7.36 (m, 2H), 7.35–7.31 (m, 1H), 7.06 (t, J = 8.8 Hz, 1H), 6.74–6.71 (m, 1H), 5.59–6.58 (m, 1H), 6.49–6.46 (m, 1H), 6.17 (br s, 1H), 4.81 (br d, J = 2.6 Hz, 1H), 4.59 (br d, J = 2.9 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 147.8, 138.9, 134.9, 130.2, 129.3, 128.6, 127.2, 118.7, 113.7, 112.0, 63.9, 51.4, 28.5 ppm. HRMS calcd. for $C_{18}H_{22}ClN_2O$ $[M+H]^+$ 317.1421; found 317.1417.

***N-tert*-Butyl-2-phenyl-2-{[3-(trifluoromethyl)phenyl)]amino]}acetamide (6e).** Yield: 220 mg (63%); white crystals; mp 137–138 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.40. IR (KBr, cm^{-1}): 3400, 3302, 1651, 1553, 1163, 1123, 696. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.41 (m, 2H), 7.40–7.37 (m, 2H), 7.36–7.32 (m, 1H), 7.24 (t, J = 7.0 Hz, 1H), 7.00–6.98 (m, 1H), 6.82–6.81 (m, 1H), 6.75–6.72 (m, 1H), 6.11 (br s, 1H), 4.98 (br d, J = 2.2 Hz, 1H), 4.64 (d, J = 2.9 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 146.8, 138.8, 131.5 (q, J = 32.1 Hz), 129.7, 129.4, 128.6, 127.2, 124.1 (q, J = 272.8 Hz), 116.6 (d, J = 1.3 Hz), 115.1 (q, J = 3.9 Hz), 110.2 (q, J = 3.8 Hz), 63.8, 51.5, 28.5 ppm. HRMS calcd. for $C_{19}H_{22}F_3N_2O$ $[M+H]^+$ 351.1684; found 351.1683.

***N-tert*-Butyl-2-[(3-phenoxyphenyl)amino]-2-phenylacetamide (6f).** Yield: 213 mg (57%); white crystals; mp 96–98 °C (*i*-Pr_2O). R_f (hexane/EtOAc 4:1) 0.43. IR (KBr, cm^{-1}): 3290, 1650, 1489, 1222, 1152, 754, 691. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.36 (m, 3H), 7.34–7.31 (m, 2H), 7.30–7.28 (m, 2H), 7.12–7.10 (m, 1H), 7.08–7.06 (m, 1H), 6.99–6.98 (m, 1H), 6.97–6.96 (m, 1H), 6.40 (dd, J_1 = 2.2 Hz, J_2 = 7.9 Hz, 1H), 6.35 (dd, J_1 = 1.9 Hz, J_2 = 8.0 Hz, 1H), 6.24 (t, J = 2.2 Hz, 1H), 6.20 (br s, 1H), 4.70 (br s, 1H), 4.57 (d, J = 2.2 Hz, 1H), 1.29 (s, 9H) ppm. ^{13}C

NMR (100 MHz, $CDCl_3$): δ 169.8, 158.5, 156.9, 148.3, 139.2, 130.2, 129.6, 129.2, 128.4, 127.2, 123.2, 119.2, 109.0, 108.7, 104.2, 64.2, 51.3, 28.5 ppm. HRMS calcd. for $C_{24}H_{27}N_2O_2$ $[M+H]^+$ 375.2072; found 375.2068.

***N-tert*-Butyl-2-phenyl-2-{[4-(trifluoromethyl)phenyl)]amino]}acetamide (6g).**[15] Yield: 195 mg (56%); white crystals; mp 173–175 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.38. IR (KBr, cm^{-1}): 3407, 3309, 1650, 1617, 1320, 1112, 1066, 826, 700. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.42 (m, 2H), 7.41–7.39 (m, 2H), 7.38–7.37 (m, 1H), 7.36–7.32 (m, 2H), 6.61–6.59 (m, 2H), 5.94 (br s, 1H), 5.23 (br d, J = 2.7 Hz, 1H), 4.67 (d, J = 3.2 Hz, 1H), 1.29 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 149.0, 138.8, 129.4, 128.7, 127.1, 126.5 (q, J = 3.8 Hz), 124.7 (q, J = 270.4 Hz), 120.0 (q, J = 32.5 Hz), 113.0, 63.2, 51.6, 28.5 ppm. HRMS calcd. for $C_{19}H_{22}F_3N_2O$ $[M+H]^+$ 351.1684; found 351.1683.

***N-tert*-Butyl-2-[(4-cyanophenyl)amino]-2-phenylacetamide (6h).** Yield: 278 mg (90%); white crystals; mp 198–199 °C (MeCN). R_f (CH_2Cl_2/MeOH 19:1) 0.60. IR (KBr, cm^{-1}): 3364, 3323, 2209, 1678, 1605, 1528, 1174, 830. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.41 (m, 2H), 7.40–7.39 (m, 2H), 7.38–7.34 (m, 3H), 6.55–6.54 (m, 1H), 6.53–6.52 (m, 1H), 5.70–5.68 (m, 2H), 4.70 (d, J = 3.8 Hz, 1H), 1.28 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.7, 149.6, 138.4, 133.6, 129.5, 128.7, 126.9, 120.1, 113.3, 99.9, 62.1, 51.8, 28.5 ppm. HRMS calcd. for $C_{19}H_{22}N_3O$ $[M+H]^+$ 308.1763; found 308.1759.

2-({[1,1'-Biphenyl]-4-yl}amino)-*N*-*tert*-butyl-2-phenylacetamide (6i). Yield: 284 mg (79%); white crystals; mp 140–141 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.34. IR (KBr, cm^{-1}): 3412, 3327, 1654, 1611, 1525, 763. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.53 (m, 1H), 7.52–7.51 (m, 1H), 7.46–7.45 (m, 2H), 7.44–7.43 (m, 2H), 7.41–7.39 (m, 2H), 7.38–7.37 (m, 2H), 7.36–7.32 (m, 1H), 7.28–7.24 (m, 1H), 6.71–6.70 (m, 1H), 6.69–6.68 (m, 1H), 6.45 (br s, 1H), 4.65 (br s, 2H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 146.1, 140.9, 139.2, 131.9, 129.2, 128.7, 128.5, 127.9, 127.3, 126.4, 126.3, 114.2, 64.7, 51.3, 28.5 ppm. HRMS calcd. for $C_{24}H_{27}N_2O$ $[M+H]^+$ 359.2123; found 359.2125.

***N-tert*-Butyl-2-[(2,4-dimethylphenyl)amino]-2-phenylacetamide (6j).** Yield: 144 mg (46%); white crystals; mp 168–169 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.47. IR (KBr, cm^{-1}): 3293, 1650, 1551, 1513, 807. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45–7.44 (m, 1H), 7.43–7.42 (m, 1H), 7.39–7.35 (m, 2H), 7.34–7.31 (m, 1H), 6.91–6.88 (m, 2H), 6.50 (br s, 1H), 6.44 (d, J = 8.0 Hz, 1H), 4.60 (s, 1H), 4.30 (br s, 1H), 2.23 (s, 3H), 2.17 (s, 3H), 1.31 (s, 9H) ppm. ^{13}C NMR (100

MHz, $CDCl_3$): δ 170.43, 142.6, 139.7, 131.0, 129.2, 128.3, 127.9, 127.4, 127.2, 123.0, 65.0, 51.1, 28.5, 20.3, 17.5 ppm. HRMS calcd. for $C_{20}H_{27}N_2O$ $[M+H]^+$ 311.2123; found 311.2115.

***N-tert*-Butyl-2-[(2,3-dihydro-1*H*-inden-5-yl)amino]-2-phenylacetamide (6k).** Yield: 203 mg (63%); white crystals; mp 142–143 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.42. IR (KBr, cm^{-1}): 3393, 3302, 2961, 1651, 1555, 1502, 699. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.39 (m, 2H), 7.38–7.35 (m, 2H), 7.34–7.30 (m, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.77 (br s, 1H), 6.55 (br d, J = 1.8 Hz, 1H), 6.44 (dd, J_1 = 2.3 Hz, J_2 = 8.0 Hz, 1H), 4.55 (s, 1H), 4.24 (br s, 1H), 2.85–2.82 (m, 2H), 2.81–2.79 (m, 2H), 2.08–2.00 (m, 2H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.6, 145.6, 145.5, 139.4, 135.0, 129.1, 128.3, 127.3, 124.7, 112.2, 110.1, 65.7, 51.0, 33.0, 31.9, 28.5, 25.6 ppm. HRMS calcd. for $C_{21}H_{27}N_2O$ $[M+H]^+$ 323.2123; found 323.2122.

***N-tert*-Butyl-2-phenyl-2-[(quinolin-5-yl)amino]acetamide (6l).** Yield: 118 mg (35%); pale yellow crystals; mp 169–171 °C (MeCN). R_f (CH_2Cl_2/MeOH 19:1) 0.23. IR (KBr, cm^{-1}): 3506, 3420, 1649, 1591, 1480, 1366, 785. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (dd, J_1 = 1.5 Hz, J_2 = 4.2 Hz, 1H), 8.37–8.35 (m, 1H), 7.53–7.52 (m, 1H), 7.51–7.50 (m, 2H), 7.46–7.43 (m, 2H), 7.42–7.38 (m, 2H), 7.37–7.34 (m, 1H), 6.47 (d, J = 7.4 Hz, 1H), 5.93 (br s, 1H), 5.83 (br d, J = 1.6 Hz, 1H), 4.81 (d, J = 2.4 Hz, 1H), 1.29 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 150.1, 149.0, 141.9, 139.0, 130.0, 129.4, 129.0, 128.7, 127.2, 119.6 (two signals), 118.8, 106.2, 63.4, 51.6, 28.5 ppm. HRMS calcd. for $C_{21}H_{23}N_3O$ $[M+H]^+$ 334.1919; found 334.1924.

***N-tert*-Butyl-2-(3-fluorophenyl)-2-(phenylamino)acetamide (6m).** Yield: 217 mg (72%); white crystals; mp 93–94 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.38. IR (KBr, cm^{-1}): 3434, 3315, 1648, 1603, 1549, 1505, 1320, 748. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.32 (m, 1H), 7.25–7.23 (m, 1H), 7.21–7.17 (m, 2H), 7.16–7.12 (m, 1H), 7.05–7.01 (m, 1H), 6.82–6.79 (m, 1H), 6.63–6.61 (m, 2H), 6.42 (br s, 1H), 4.61 (br d, J = 2.5 Hz, 1H), 4.54 (br s, 1H), 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.5, 163.2 (d, J =247.2 Hz), 146.4, 141.8 (d, J = 6.8 Hz), 130.7 (d, J = 8.1 Hz), 129.3, 123.1 (d, J = 2.9 Hz), 119.2, 115.4 (d, J = 21.3 Hz), 114.2 (d, J = 22.0 Hz), 113.9, 64.2 (d, J = 4.1 Hz), 51.3, 28.5 ppm. HRMS calcd. for $C_{18}H_{22}FN2O$ $[M+H]^+$ 301.1716; found 301.1712.

***N-tert*-Butyl-2-(phenylamino)-2-[3-(trifluoromethyl)phenyl]acetamide (6n).** Yield: 240 mg (69%); white crystals; mp 105–106 °C (hexane). R_f (hexane/EtOAc 4:1) 0.43. IR (KBr, cm^{-1}): 3321, 1643, 1332, 1122, 751. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (s, 1H), 7.63–7.59 (m, 2H), 7.50 (t, J = 7.8 Hz, 1H), 7.22–7.18 (m, 2H), 6.85–6.81 (m, 1H), 6.65–6.62 (m, 2H), 6.54 (br s,

1H), 4.68 (s, 1H), 4.46 (br s, 1H), 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 146.3, 140.2, 131.5 (q, J = 32.4 Hz), 130.8 (d, J = 1.4 Hz), 129.7, 129.4, 125.3 (q, J = 3.7 Hz), 124.1 (q, J = 3.8 Hz), 123.8 (q, J = 272.8 Hz), 119.5, 113.9, 64.4, 51.4, 28.5 ppm. HRMS calcd. for $C_{19}H_{21}F_3N_2O$ $[M+H]^+$ 351.1684; found 351.1680.

***N-tert*-Butyl-2-(3-phenoxyphenyl)-2-(phenylamino)acetamide (6o).** Yield: 297 mg (79%); pale yellow oil. R_f (hexane/EtOAc 4:1) 0.43. IR (film, cm^{-1}): 3320, 1672, 1600, 1497, 744, 693. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.33 (m, 2H), 7.32–7.31 (m, 1H), 7.20–7.16 (m, 2H), 7.14–7.10 (m, 2H), 7.07–7.05 (m, 1H), 7.02–7.01 (m, 1H), 7.00–6.99 (m, 1H), 6.98–6.95 (m, 1H), 6.82–6.78 (m, 1H), 6.62–6.60 (m, 2H), 6.47 (br s, 1H), 4.56 (d, J = 2.3 Hz, 1H), 4.46 (br d, J = 1.6 Hz, 1H), 1.29 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 158.0, 156.6, 146.6, 141.2, 130.5, 129.8, 129.2, 123.6, 122.1, 119.2, 119.1, 118.5, 117.1, 113.9, 64.6, 51.2, 28.5 ppm. HRMS calcd. for $C_{24}H_{27}N_2O_2$ $[M+H]^+$ 375.2072; found 375.2067.

***N-tert*-Butyl-2-(phenylamino)-2-[4-(trifluoromethyl)phenyl]acetamide (6p).** Yield: 244 mg (70%); white crystals; mp 140–141 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.30. IR (KBr, cm^{-1}): 3296, 1651, 1603, 1506, 1363, 1128, 748, 692. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66–7.63 (m, 2H), 7.57–7.55 (m, 2H), 7.22–7.18 (m, 2H), 6.84–6.80 (m, 1H), 6.63–6.61 (m, 2H), 6.44 (br s, 1H), 4.68 (s, 1H), 4.53 (br s, 1H), 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 146.3, 143.2, 130.4 (q, J = 33.0 Hz), 129.4, 127.7, 126.2 (q, J = 3.5 Hz), 123.9 (q, J = 272.2 Hz), 119.4, 113.9, 64.3, 51.4, 28.5 ppm. HRMS calcd. for $C_{19}H_{22}F_3N_2O$ $[M+H]^+$ 351.1684; found 351.1681.

2-{[1,1'-Biphenyl]-4-yl}-*N-tert*-butyl-2-(phenylamino)acetamide (6q). Yield: 268 mg (75%); white crystals; mp 125–126 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.37. IR (KBr, cm^{-1}): 3364, 2967, 1666, 1605, 1505, 755, 694. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.59 (m, 2H), 7.58–7.57 (m, 2H), 7.50–7.48 (m, 2H), 7.45–7.42 (m, 2H), 7.37–7.33 (m, 1H), 7.22–7.18 (m, 2H), 6.83–6.79 (m, 1H), 6.67–6.64 (m, 2H), 6.58 (br s, 1H), 4.65 (d, J = 2.3 Hz, 1H), 4.52 (br d, J = 1.8 Hz, 1H), 1.34 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 146.8, 141.4, 140.5, 138.2, 129.3, 128.8, 127.9, 127.7, 127.5, 127.1, 119.1, 113.9, 64.6, 51.2, 28.6 ppm. HRMS calcd. for $C_{24}H_{27}N_2O$ $[M+H]^+$ 359.2123; found 359.2123.

***N-tert*-Butyl-2-(naphthalen-2-yl)-2-(phenylamino)acetamide (6r).** Yield: 295 mg (89%); white crystals; mp 148–149 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.37. IR (KBr, cm^{-1}): 3367, 2931, 1668, 1607, 1508, 748. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.89 (m, 1H), 7.87–7.85 (m,

2H), 7.83–7.81 (m, 1H), 7.53–7.48 (m, 3H), 7.20–7.16 (m, 2H), 6.80–6.77 (m, 1H), 6.67–6.65 (m, 2H), 6.44 (s, 1H), 4.78 (d, J = 2.3 Hz), 4.71 (s, 1H), 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 146.8, 136.8, 133.4, 133.2, 129.3, 129.2, 128.0, 127.7, 126.6, 126.5, 126.3, 124.7, 119.0, 113.9, 64.7, 51.3, 28.6 ppm. HRMS calcd. for $C_{22}H_{25}N_2O$ $[M+H]^+$ 333.1967; found 333.1963.

***N-tert*-Butyl-2-(9*H*-fluoren-2-yl)-2-(phenylamino)acetamide (6s).** Yield: 249 mg (67%); white crystals; mp 149.5–151.5 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.35. IR (KBr, cm^{-1}): 3357, 1671, 1605, 1514, 750, 735, 692. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79–7.76 (m, 2H), 7.61–7.59 (m, 1H), 7.55–7.53 (m, 1H), 7.45–7.42 (m, 1H), 7.39–7.35 (m, 1H), 7.32–7.29 (m, 1H), 7.20–7.16 (m, 2H), 6.81–6.77 (m, 1H), 6.66–6.64 (m, 2H), 6.49 (s, 1H), 4.67 (d, J = 1.6 Hz, 1H), 4.62 (s, 1H), 3.90 (s, 2H), 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 146.9, 144.2, 143.4, 142.1, 141.1, 137.9, 129.2, 127.0, 126.8, 125.9, 125.1, 124.0, 120.4, 120.0, 119.0, 113.9, 64.9, 51.2, 36.9, 28.6 ppm. HRMS calcd. for $C_{25}H_{27}N_2O$ $[M+H]^+$ 371.2123; found 371.2120.

***N-tert*-Butyl-2-(furan-2-yl)-2-(phenylamino)acetamide (6t).** Yield: 143 mg (53%); white crystals; mp 125–126 °C (*i*-Pr_2O). R_f (hexane/EtOAc 4:1) 0.35. IR (KBr, cm^{-1}): 3295, 1649, 1604, 1551, 1509, 748, 691. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.39 (m, 1H), 7.22–7.18 (m, 2H), 6.83–6.79 (m, 1H), 6.65–6.63 (m, 2H), 6.53 (br s, 1H), 6.37–6.35 (m, 1H), 4.76 (d, J = 3.0 Hz, 1H), 4.66 (br s, 1H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 151.2, 146.4, 142.5, 129.3, 119.2, 113.8, 110.8, 108.0, 58.5, 51.3, 28.5 ppm. HRMS calcd. for $C_{16}H_{21}N_2O_2$ $[M+H]^+$ 273.1603; found 273.1601.

***N-tert*-butyl-2-(phenylamino)-2-(pyridin-3-yl)acetamide (6u).** Yield: 240 mg (85%); white crystals; mp 149.5–151.5 °C (hexane−EtOAc). R_f (CH_2Cl_2/MeOH 19:1) 0.19. IR (KBr, cm^{-1}): 3330, 2967, 1659, 1603, 1485, 1248, 750, 691. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, J = 2.1 Hz, 1H), 8.58 (dd, J_1 = 1.5 Hz, J_2 = 4.8 Hz, 1H), 7.76–7.72 (m, 1H), 7.32–7.29 (m, 1H), 7.22–7.18 (m, 2H), 6.84–6.81 (m, 1H), 6.65–6.63 (m, 2H), 6.57 (br s, 1H), 4.66 (d, J = 3.0 Hz, 1H), 4.52 (br d, J = 2.6 Hz, 1H), 1.32 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 149.7, 148.9, 146.2, 135.0, 134.8, 129.4, 123.9, 119.4, 113.9, 62.4, 51.4, 28.5 ppm. HRMS calcd. for $C_{17}H_{22}N3O$ $[M+H]^+$ 284.1763; found 284.1755.

***N-tert*-Butyl-2-(phenylamino)-2-(quinolin-4-yl)acetamide (6v).** Yield: 228 mg (68%); white crystals; mp 153–155 °C (hexane−EtOAc). R_f (CH_2Cl_2/MeOH 19:1) 0.40. IR (KBr, cm^{-1}): 3352, 2969, 1674, 1652, 1604, 1510, 748. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.89–8.88 (m, 1H), 8.17–8.15

(m, 1H), 8.02–8.00 (m, 1H), 7.76–7.72 (m, 1H), 7.59–7.55 (m, 1H), 7.45–7.44 (m, 1H), 7.25–7.20 (m, 2H), 6.88–6.85 (m, 1H), 6.71–6.67 (m, 3H), 5.36 (d, *J* = 2.9 Hz, 1H), 4.59 (br d, *J* = 2.5 Hz, 1H), 1.35 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 169.1, 150.4, 148.8, 146.5, 144.3, 130.7, 129.6, 129.5, 127.5, 126.5, 123.0, 119.7, 119.3, 113.9, 60.6, 51.6, 28.5 ppm. HRMS calcd. for $C_{21}H_{24}N_3O$ $[M+H]^+$ 334.1919; found 334.1916.

2-({[1,1'-Biphenyl]-4-yl}amino)-*N*-*tert*-butyl-2-[4-(trifluoromethyl)phenyl]acetamide (6w). Yield: 280 mg (66%); white crystals; mp 167–168 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.40. IR (KBr, cm^{-1}): 3406, 3336, 1651, 1612, 1490, 1328, 1120, 761. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.67–7.65 (m, 2H), 7.59–7.57 (m, 2H), 7.53–7.51 (m, 2H),7.46–7.43 (m, 2H), 7.41–7.37 (m, 2H), 7.29–7.25 (m, 1H), 6.70–6.67 (m, 2H), 6.39 (br s, 1H), 4.73 (br d, *J* = 2.7 Hz, 1H), 4.67 (br d, *J* = 2.4 Hz, 1H), 1.33 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 169.2, 145.6, 143.2, 140.7, 132.3, 130.7 (q, *J* = 32.3 Hz), 128.7, 128.0, 127.7, 126.5, 126.4, 126.2 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.2 Hz), 114.2, 64.1, 51.5, 28.5 ppm. HRMS calcd. for $C_{25}H_{26}F_3N_2O$ $[M+H]^+$ 427.1997; found 427.1998.

2-{[1,1'-Biphenyl]-4-yl}-*N*-*tert*-butyl-2-[(4-cyanophenyl)amino]acetamide (6x). Yield: 302 mg (79%); white crystals; mp 125–127 °C (hexane−EtOAc). R_f (hexane/EtOAc 4:1) 0.17. IR (KBr, cm^{-1}): 3338, 2966, 2213, 1678, 1606, 1523, 1175, 825, 758. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.67–7.65 (m, 2H), 7.59–7.57 (m, 2H), 7.53–7.51 (m, 2H), 7.46–7.43 (m, 2H), 7.41–7.37 (m, 2H), 7.29–7.25 (m, 1H), 6.70–6.67 (m, 2H), 5.72 (br s, 1H), 5.69 (br d, *J* = 2.7 Hz, 1H), 4.74 (br d, *J* = 2.4 Hz, 1H), 1.30 (s, 9H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 168.9, 149.6, 141.7, 140.1, 137.3, 133.8, 128.8, 128.1, 127.7, 127.3, 127.0, 120.1, 113.4, 100.1, 61.9, 51.9, 28.5 ppm. HRMS calcd. for $C_{25}H_{26}N3O$ $[M+H]^+$ 384.2076; found 384.2073.

***N*-Pentyl-2-phenyl-2-(phenylamino)acetamide (6y).** Yield: 263 mg (89%); colorless oil. R_f (hexane/EtOAc 4:1) 0.30. IR (film, cm^{-1}): 3311, 2931, 1652, 1602, 1504, 1315, 749, 649. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.44–7.42 (m, 2H), 7.39–7.35 (m, 2H), 7.34–7.31 (m, 1H), 7.20–7.16 (m, 2H), 6.81–6.77 (m, 1H), 6.70 (br t, *J* = 6.4 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 2H), 4.72 (d, *J* = 2.2 Hz, 1H), 4.55 (br d, *J* = 1.3 Hz, 1H), 3.28–3.22 (m, 2H), 1.48–1.40 (m, 2H), 1.28–1.22 (m, 2H), 1.20–1.13 (m, 2H), 0.83 (t, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.9, 146,7, 139.0, 129.3, 129.2, 128.5, 127.3, 119.0, 113.8, 64.2, 39.4, 29.1, 28.9, 22.2, 13.9 ppm. HRMS calcd. for $C_{19}H_{25}N_2O$ $[M+H]^+$ 297.1967; found 297.1960.

2-[(4-Fluorophenyl)amino]-*N*-pentyl-2-phenylacetamide (6z). Yield: 148 mg (47%); colorless oil. R_f (hexane/EtOAc 4:1) 0.27. IR (film, cm^{-1}): 3308, 2932, 1652, 1510, 1222, 821, 698. ^1H NMR (400 MHz, $CDCl_3$): δ 7.44–7.42 (m, 2H), 7.40–7.37 (m, 2H), 7.36–7.32 (m, 1H), 6.90–6.86 (m, 2H), 6.57–6.54 (m, 3H), 4.66 (br s, 1H), 4.53 (br s, 1H), 3.28–3.23 (m, 2H), 1.48–1.40 (m, 2H), 1.28–1.22 (m, 2H), 1.20–1.13 (m, 2H), 0.83 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 156.6 (d, J = 237.0 Hz), 143.0 (d, J = 2.0 Hz), 138.9, 129.3, 128.6, 127.3, 115.8 (d, J = 22.6 Hz), 114.7 (d, J = 7.6 Hz), 64.6, 39.5, 29.1, 28.9, 22.2, 13.9 ppm. HRMS calcd. for $C_{19}H_{24}FN_2O$ $[M+H]^+$ 315.1873; found 315.1869.

2-[(4-Cyanophenyl)amino]-*N*-pentyl-2-phenylacetamide (6aa). Yield: 201 mg (63%); colorless oil. R_f (CH_2Cl_2/MeOH 19:1) 0.60. IR (film, cm^{-1}): 3355, 2931, 2215, 1659, 1606, 1519, 1335, 1174, 826, 698, 545. ^1H NMR (400 MHz, $CDCl_3$): δ 7.43–7.41 (m, 2H), 7.40–7.38 (m, 2H), 7.37–7.32 (m, 3H), 6.56–6.53 (m, 2H), 5.89–5.86 (m, 1H), 5.72 (d, J = 3.4 Hz, 1H), 4.79 (d, J = 3.7 Hz, 1H), 3.26–3.20 (m, 2H), 1.43–1.39 (m, 2H), 1.26–1.20 (m, 2H), 1.17–1.11 (m, 2H), 0.83 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 149.6, 138.2, 133.6, 129.5, 128.9, 127.0, 120.0, 113.4, 100.0, 61.8, 39.9, 29.0, 28.7, 22.2, 13.9 ppm. HRMS calcd. for $C_{20}H_{24}N_3O$ $[M+H]^+$ 322.1919; found 322.1916.

2-(Naphthalen-2-yl)-*N*-pentyl-2-(phenylamino)acetamide (6ab). Yield: 310 mg (89%); colorless oil. R_f (hexane/EtOAc 4:1) 0.42. IR (film, cm^{-1}): 3312, 2932, 1660, 1504, 1316, 750, 478. ^1H NMR (400 MHz, $CDCl_3$): δ 7.91–7.90 (m, 1H), 7.86–7.83 (m, 2H), 7.82–7.81 (m, 1H), 7.52 (dd, J_1 = 1.8 Hz, J_2 = 10.2 Hz, 1H), 7.50–7.46 (m, 2H), 7.19–7.15 (m, 2H), 6.80–6.76 (m, 1H), 6.67–6.62 (m, 3H), 4.90 (d, J = 2.1 Hz, 1H), 4.75 (br d, J = 1.4 Hz, 1H), 3.31–3.20 (m, 2H), 1.47–1.39 (m, 2H), 1.26–1.20 (m, 2H), 1.19–1.13 (m, 2H), 0.81 (t, J = 6.9 Hz, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 146.7, 136.5, 133.4, 133.2, 129.3, 129.2, 127.9, 127.7, 126.6, 126.5, 126.4, 124.8, 119.0, 113.9, 64.1, 39.6, 29.1, 28.9, 22.2, 13.9 ppm. HRMS calcd. for $C_{23}H_{27}N_2O$ $[M+H]^+$ 347.2123; found 347.2122.

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