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Catalyst-Free Synthesis of α-Aminoacyl-amides via N,N'-Bis(Phenylmethylidene)phenylmethanediam as Imine Surrogate in Ugi Multicomponent Reaction

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# CATALYST-FREE SYNTHESIS OF α-AMINOACYL-AMIDES VIA N,N'-BIS(PHENYLMETHYLIDENE) PHENYLMETHANEDIAMINE AS IMINE SURROGATE IN UGI MULTICOMPONENT REACTION

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#### GRAPHICAL ABSTRACT

**Abstract** A novel one-pot, multicomponent, and catalyst-free reaction of N,N'-bis (phenylmethylidene) phenylmethane, carboxylic acids, and isocyanides yielding  $\alpha$ -aminoacyl-amides is described. The reaction is based on the combination of an Ugi three-component reaction followed by hydrolysis.

Keywords Diimine; isocyanide; three-component reaction; Ugi reaction

#### INTRODUCTION

Multicomponent reactions (MCRs) have recently become one of the favored methods to prepare pharmacologically relevant compounds.<sup>[1]</sup> Among many kinds of multicomponent condensations, the Ugi reaction,<sup>[2]</sup> discovered more than 40 years ago, is without any doubt the most widely exploited, not only to prepare peptide-like molecules but also to achieve many different types of biologically active targets.<sup>[3]</sup> The large range of structures accessible through this powerful reaction is continually expanding, through ongoing development of variations of the MCR, together with an increasing number of elaborate post-condensation modifications and cascade processes.<sup>[4-6]</sup> Despite such widespread application, use of diimines as readily available nitrogen source in the Ugi three-component condensation (3-CC) has received comparatively little attention. Diimines serve as a good precursor for the synthesis of numerous organic compounds, especially aza-cyclic compounds.<sup>[7-12]</sup> This easily accessible precursor can be produced by the reaction of aromatic aldehydes and ammonia solution. As part of our continuing effort to design new routes for the

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**Table 1.** Reaction of N, N'-bis(phenylmethylidene)phenylmethanediamine, carboxylic acids 1, and isocyanides 2

3	R	R'	Yield of <b>3</b> (%)
a	Bn	t-Bu	98
b	Bn	Cyclohexyl	94
c	Ph <sub>2</sub> CH-	t-Bu	95
d	Ph <sub>2</sub> CH-	Cyclohexyl	93
e	Cinammyl	<i>t</i> -Bu	92
f	Cinammyl	Cyclohexyl	96
g	P-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	t-Bu	95
h	P-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	Cyclohexyl	94
i	Furyl	t-Bu	96
j	Furyl	Cyclohexyl	98

preparation of biologically active compounds, [13–16] herein we describe a simple, one-pot, three-component synthesis of  $\alpha$ -aminoacyl-amides derivatives. The reaction of N, N'-bis(phenylmethylidene)phenylmethanediamine and carboxylic acid  $\mathbf{1}$  in the presence of isocyanides  $\mathbf{2}$  in anhydrous toluene at reflux condition produces title compound  $\mathbf{3}$  in 92–98% yields (Table 1).

#### RESULTS AND DISCUSSION

Regarding the well-documented general mechanism of the Ugi reaction,  $[^{2,5]}$  we proposed a five-key-step plausible mechanism for the mentioned reaction (Scheme 1). The first step begins through a protonation of N, N'-bis(phenylmethylidene)phenylmethanediamine to produce iminium salt 4. Then isocyanide 2 is subsequently added to the iminium salt 4 to produce the reactive nitrilium intermediate 5. The reactive O-acyl iminolate 6 is formed via the  $\alpha$ -addition of the carboxylate anion to the nitrilium ion 5. Another step involves O- to N-acyl transfer (Mumm rearrangement) to afford the intermediate 7. Finally, intermediate 7 in the presence of air, moisture, or water is converted to product 3. To our delight, we found that the desired product could be isolated in all cases with good to quantitative yields.

The structures of compounds **3a**–**j** were deduced from their elemental analysis, infrared (IR), and high-field <sup>1</sup>H and <sup>13</sup>C NMR spectra.

**Scheme 1.** Proposed mechanism for the formation of  $\alpha$ -aminoacyl-amide.

#### CONCLUSION

In summary, we have demonstrated that the one-pot, three-component Ugi reaction of diimine, carboxcylic acides, and isocyanide provides a simple method for the preparation of  $\alpha$ -aminoacyl-amides of potential synthetic. Fairly good yields of the products without any activation, the ready availability of the starting materials, the reaction's simplicity, and its mild conditions are the main advantages of this method.

#### **EXPERIMENTAL**

All chemicals were obtained from Merck (Germany) and Fluka (Switzerland). <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured (CDCl<sub>3</sub> solution) with a Bruker DRX-500 Avance spectrometer at 500.13 and 125.75 MHz, respectively. IR spectra were recorded on a Shimadzu IR-460 spectrometer. Chromatography columns were prepared from Merck silica gel, 230–240 mesh. Mass spectra were obtained using a Finnigan-Mat 8430 spectrometer operating at an ionization potential of 70 eV.

# Typical Procedure for Preparation of *N'*-(*tert*-Butyl)-2-phenyl-2-[(2-phenylacetyl)amino]acetamide (3a)

To a magnetically stirred solution of  $NH_4OH$  (30%, 5 mL), 0.16 g benzal-dehyde (1.5 mmol) was added, and the solution was stirred for 5 h at reflux. During this time, a white precipitate formed. The precipitate was removed by filtration and dried. The solid was dissolved in toluene (5 mL), and 0.14 g 2-phenylacetic acid

(1 mmol) and 0.08 g *tert*-butyl isocyanide (1 mmol) were added to the mixture. The resulting solution was stirred for 12 h at reflux. When the reaction mixture was cooled to room temperature, a white solid precipitated. The precipitates were filtered and washed with diethyl ether to give product **3a** in 98% yields. All products gave satisfactory spectral data in accordance with the assigned structures (0.32 g, 98%).

## N<sup>1</sup>-(tert-Butyl)-2-phenyl-2-[(2-phenylacetyl)amino]acetamide (3a)

Yield: 0.32 g (98%); white crystals; mp = 184–186 °C. IR (KBr): 3287 (NH), 1636 (C=O), 1558 and 1494 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.24 (9 H, s,  $Me_3$ C), 3.57 (2 H, s, CH<sub>2</sub>), 5.38 (1 H, d,  $^3J_{\rm HH}$  = 7.0 Hz, CH), 5.69 (1 H, s, NH), 6.92 (1 H, d,  $^3J_{\rm HH}$  = 6.4 Hz, NH), 7.23–7.34 ppm (10 H, m, 10 CH of Ar). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 28.53 ( $Me_3$ C), 43.60 (CH<sub>2</sub>), 51.74 ( $Me_3$ C), 57.34 (CH), 127.11 (2 CH of Ar), 127.24 (CH of Ar), 128.13 (CH of Ar), 128.87 (2 CH of Ar), 128.90 (2 CH of Ar), 129.29 (2 CH of Ar), 134.67 (C<sub>ipso</sub>-CH<sub>2</sub>), 138.54 (C<sub>ipso</sub>-CH), 168.83 (C=O), 170.25 ppm (C=O). MS (EI, 70 eV): m/z (%) = 324 (M<sup>+</sup>, 4), 224 (35), 210 (42), 105 (73), 91 (50), 71 (65), 57 (100), 43 (92). Anal. calcd. for C<sub>20</sub>H<sub>24</sub>N<sub>2</sub>O<sub>2</sub> (324.42): C, 74.05; H, 7.46; N, 8.63%. Found: C, 74.07; H, 7.47; N, 8.64%.

## N<sup>1</sup>-Cyclohexyl-2-phenyl-2-[(2-phenylacetyl)amino]acetamide (3b)

Yield: 0.33 g (94%); white crystals; mp = 244–246 °C. IR (KBr): 3305 (NH), 1681 and 1631 (C=O), 1525 and 1493 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 0.84–1.86 (10 H, m, 5 CH<sub>2</sub> of cyclohexyl), 3.58 (2 H, s, CH<sub>2</sub>), 3.72 (1 H, m, CH), 5.33 (1 H, d,  ${}^3J_{\rm HH}$  = 6.8 Hz, CH), 5.37 (1 H, d,  ${}^3J_{\rm HH}$  = 7.3 Hz, NH), 6.84 (1 H, d,  ${}^3J_{\rm HH}$  = 5.7 Hz, NH), 7.25–7.39 ppm (10 H, m, 10 CH of Ar). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 24.53 (CH<sub>2</sub>), 24.67 (CH<sub>2</sub>), 25.36 (CH<sub>2</sub>), 32.58 (CH<sub>2</sub>), 32.77 (CH<sub>2</sub>), 41.67 (CH<sub>2</sub>), 48.72 (CH), 57.18 (CH), 125.3 (2 CH of Ar), 127.22 (CH of Ar), 127.32 (CH of Ar), 128.94 (2 CH of Ar), 128.97 (2 CH of Ar), 129.34 (2 CH of Ar), 134.60 ( $C_{ipso}$ -CH<sub>2</sub>), 138.31 ( $C_{ipso}$ -CH), 168.65 (C=O), 170.28 ppm (C=O). MS (EI, 70 eV): m/z (%) = 350 (M<sup>+</sup>, 1), 259 (1), 225 (100), 188 (5), 106 (74), 91 (80), 77 (8), 55 (18), 41 (12). Anal. calcd. for  $C_{22}H_{26}N_2O_2$  (350.46): C, 75.40; H, 4.48; N, 7.99%. Found: C, 75.48; H, 4.52; N, 8.01%.

# $N^1$ -(tert-Butyl)-2-[(2,2-diphenylacetyl)amino]-2-phenylacetamide (3c)

Yield: 0.38 g (95%); white crystals; mp = 246–248 °C. IR (KBr): 3290 (NH), 1636 (C=O), 1547 and 1491 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.21 (9 H, s,  $Me_3$ C), 4.95 (1 H, s, CH), 5.40 (1 H, d,  $^3J_{\rm HH}$  = 6.8 Hz, CH), 5.65 (1 H, s, NH), 7.05 (1 H, d,  $^3J_{\rm HH}$  = 7.4 Hz, NH), 7.18–7.30 ppm (15 H, m, 15 CH of Ar). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 28.50 ( $Me_3$ C), 51.74 ( $Me_3$ C), 57.64 (CH), 58.78 (CH), 127.16 (2 CH of Ar), 127.19 (CH of Ar), 127.22 (CH of Ar), 128.15 (CH of Ar), 128.68 (2 CH of Ar), 128.80 (2 CH of Ar), 128.88 (2 CH of Ar), 128.94 (2 CH of Ar), 129.24 (2 CH of Ar), 138.36 ( $C_{ipso}$ -CH), 139.18 ( $C_{ipso}$ -CH), 139.24 ( $C_{ipso}$ -CH), 168.72 (C=O), 171.27 ppm (C=O). MS (EI, 70 eV): m/z (%) = 401 (M<sup>+</sup> + 1, 1), 301 (58), 233 (23), 167 (100), 152 (16), 134 (27), 106 (53),

91 (8), 57 (22), 41 (9). Anal. calcd. for  $C_{26}H_{28}N_2O_2$  (400.52): C, 77.97; H, 7.05; N, 6.99%. Found: C, 77.98; H, 7.07; N, 6.99%.

## N<sup>1</sup>-Cyclohexyl-2-[(2,2-diphenylacetyl)amino]-2-phenylacetamide (3d)

Yield: 0.4 g (93%); white crystals; mp = 220–222 °C. IR (KBr): 3285 (NH), 1632 (C=O), 1542 and 1491 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 0.86–1.80 (10 H, m, 5 CH<sub>2</sub> of cyclohexyl), 3.66 (1 H, m, CH), 4.96 (1 H, s, CH), 5.45 (1 H, d,  $^3J_{\rm HH}$  = 6.7 Hz, CH), 5.64 (1 H, br, NH), 7.06 (1 H, d,  $^3J_{\rm HH}$  = 6.65 Hz, NH), 7.21–7.35 ppm (15 H, m, 15 CH of Ar). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 24.54 (CH<sub>2</sub>), 24.69 (CH<sub>2</sub>), 25.35 (CH<sub>2</sub>), 32.52 (CH<sub>2</sub>), 32.69 (CH<sub>2</sub>), 48.69 (CH of cyclohexyl), 57.37 (CH), 58.86 (CH), 127.23 (4 CH of Ar), 128.26 (CH of Ar), 128.67 (2 CH of Ar), 128.71 (2 CH of Ar), 128.83 (2 CH of Ar), 128.92 (4 CH of Ar), 138.24 (C<sub>ipso</sub>-CH), 139.16 (C<sub>ipso</sub>-CH), 139.24 (C<sub>ipso</sub>-CH), 168.59 (C=O), 171.29 ppm (C=O). MS (EI, 70 eV): m/z (%) = 427 (M<sup>+</sup> + 1, 1), 301 (66), 259 (53), 188 (32), 167 (100), 152 (16), 106 (57), 55 (18), 41 (9). Anal. calcd. for C<sub>28</sub>H<sub>30</sub>N<sub>2</sub>O<sub>2</sub> (426.56): C, 78.84; H, 7.09; N, 6.57%. Found: C, 59.98; H, 7.82; N, 4.81%.

# (*E*)-*N*<sup>1</sup>-[2-(*tert*-Butylamino)-2-oxo-1-phenylethyl]-3-phenyl-2-propenamide (3e)

Yield: 0.31 g (92%); white crystals; mp = 234–236 °C. IR (KBr): 3290 (NH), 1643 and 1618 (C=O), 1547 and 1495 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.31 (9 H, s,  $Me_{\rm 3}$ C), 5.58 (1 H, d,  $^3J_{\rm HH}$  = 8.4 Hz, CH), 5.79 (1 H, s, NH), 6.49 (1 H, d,  $^3J_{\rm HH}$  = 15.7 Hz, CH), 7.21 (1 H, d,  $^3J_{\rm HH}$  = 7.4 Hz, NH), 7.26–7.47 (10 H, m, 10 CH of Ar), 7.59 ppm (1 H, d,  $^3J_{\rm HH}$  = 15.7 Hz, CH). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 28.60 ( $Me_{\rm 3}$ C), 51.89 ( $Me_{\rm 3}$ C), 57.37 (CH), 120.53 (CH=CHCO), 127.31 (2 CH of Ar), 127.84 (2 CH of Ar), 128.22 (CH of Ar), 128.81 (2 CH of Ar), 128.99 (2 CH of Ar), 129.72 (CH of Ar), 134.81 ( $C_{ipso}$ -C=C), 138.64 ( $C_{ipso}$ -CH), 141.43 ( $C_{\rm H}$ =CHCO), 165.15 (C=O), 169.15 ppm (C=O). MS (EI, 70 eV): m/z (%) = 337 ( $M^+$  + 1, 1), 237 (85), 193 (5), 131 (100), 103 (38), 90 (2), 77 (22), 57 (14), 41 (7). Anal. calcd. for  $C_{\rm 21}H_{\rm 24}N_{\rm 2}O_{\rm 2}(336.43)$ : C, 74.97; H, 7.19; N, 8.33%. Found: C, 74.9; H, 7.25; N, 8.38%.

# (E)-N¹-[2-(Cyclohexylamino)-2-oxo-1-phenylethyl]-3-phenyl-2-propenamide (3f)

Yield: 0.35 g (96%); white crystals; mp = 251–252 °C. IR (KBr): 3277 (NH), 1643 and 1615 (C=O), 1547 and 1449 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.03–1.93 (10 H, m, 5 CH<sub>2</sub> of cyclohexyl), 3.76–3.78 (1 H, m, CH), 5.57 (1 H, d,  ${}^3J_{\rm HH}$  = 6.9 Hz, CH), 5.68 (1 H, d,  ${}^3J_{\rm HH}$  = 7.7 Hz, NH), 6.5 (1 H, d,  ${}^3J_{\rm HH}$  = 15.6 Hz, Hz, CH), 7.15 (1 H, d,  ${}^3J_{\rm HH}$  = 6.5 Hz, NH), 7.26–7.49 (10 H, m, 10 CH of Ar), 7.60 ppm (1 H, d,  ${}^3J_{\rm HH}$  = 15.6 Hz, CH). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 24.59 (CH<sub>2</sub>), 24.70 (CH<sub>2</sub>), 25.41 (CH<sub>2</sub>), 32.65 (CH<sub>2</sub>), 32.83 (CH<sub>2</sub>), 48.82 (CH), 57.24 (CH), 120.39 (CH=CHCO), 127.37 (2 CH of Ar), 127.86 (2 CH of Ar), 128.32 (CH of Ar), 128.82 (2 CH of Ar), 129.02 (2 CH of Ar), 129.75 (CH of Ar), 134.79 (C<sub>ipso</sub>-C=C), 138.43 (C<sub>ipso</sub>-CH), 141.58 (CH=CHCO), 165.18 (C=O), 168.94 ppm

(C=O). MS (EI, 70 eV): m/z (%) = 363 (M<sup>+</sup> + 1, 2), 237 (100), 193 (4), 131 (97), 103 (33), 77 (17), 55 (11). Anal. calcd. for  $C_{23}H_{26}N_2O_2(362.47)$ : C, 76.21; H, 7.23; N, 7.73%. Found: C, 76.22; H, 7.25; N, 7.72%.

## N<sup>1</sup>-[2-(tert-Butylamino)-2-oxo-1-phenylethyl]-4-nitrobenzamide (3g)

Yield: 0.34 g (95%); white crystals; mp = 260–262 °C. IR (KBr): 3325 (NH), 1671 and 1636 (C=O), 1547 and 1522 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.31 (9 H, s,  $Me_{\rm 3}$ C), 5.49 (1 H, s, NH), 5.50 (1 H, q,  $^3J_{\rm HH}$  = 3.4 Hz, CH), 7.26–7.40 (3 H, m, CH of Ar), 7.46 (2 H, d,  $^3J_{\rm HH}$  = 8.5 Hz, CH of Ar), 7.85 (1 H, br, NH), 7.98 (2 H, d,  $^3J_{\rm HH}$  = 8.8 Hz, CH of Ar), 8.26 ppm (2 H, d,  $^3J_{\rm HH}$  = 8.8 Hz, CH of Ar). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 28.55 ( $Me_{\rm 3}$ C), 52.16 ( $Me_{\rm 3}$ C), 57.77 (CH), 123.72 (2 CH of Ar), 127.41 (2 CH of Ar), 128.37 (2 CH of Ar), 128.63 (CH of Ar), 129.22 (2 CH of Ar), 138.17 ( $C_{ipso}$ -CH), 139.50 ( $C_{ipso}$ -C=O), 149.75 ( $C_{ipso}$ -NO<sub>2</sub>), 164.34 (C=O), 168.62 ppm (C=O). MS (EI, 70 eV): m/z (%) = 313 (2), 256 (100), 239 (6), 209 (8), 150 (89), 120 (12), 104 (53), 76 (25), 57 (41), 41 (19). Anal. calcd. for  $C_{19}H_{21}N_{3}O_{4}$  (355.39): C, 64.21; H, 5.96; N, 11.82%. Found: C, 64.22; H, 5.97; N, 11.83%.

#### N<sup>1</sup>-[2-(Cyclohexylamino)-2-oxo-1-phenylethyl]-4-nitrobenzamide (3h)

Yield: 0.36 g (94%); white crystals; mp = 200–202 °C. IR (KBr): 3282 (NH), 1632 (C=O), 1543 and 1516 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.07–1.77 (m, 10 H, 5 CH<sub>2</sub> of cyclohexyl), 3.52–3.54 (1 H, m, CH), 5.69 (1 H, d,  ${}^3J_{\rm HH}$  = 8.1 Hz, CH), 7.27 (1 H, d,  ${}^3J_{\rm HH}$  = 7.2 Hz, NH), 7.34 (2 H, d,  ${}^3J_{\rm HH}$  = 7.6 Hz, 2 CH of Ar), 7.50 (2 H, d,  ${}^3J_{\rm HH}$  = 7.5 Hz, 2 CH of Ar), 8.13 (2 H, t,  ${}^3J_{\rm HH}$  = 8.6 Hz, 2 CH of Ar), 8.23 (1 H, t,  ${}^3J_{\rm HH}$  = 7.2 Hz, CH of Ar), 8.27 (2 H, d,  ${}^3J_{\rm HH}$  = 8.6 Hz, 2 CH of Ar), 9.23 ppm (1 H, d,  ${}^3J_{\rm HH}$  = 8.0 Hz, NH). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 24.33 (CH<sub>2</sub>), 24.44 (CH<sub>2</sub>), 25.13 (CH<sub>2</sub>), 32.12 (CH<sub>2</sub>), 32.20 (CH<sub>2</sub>), 47.75 (CH), 57.02 (CH), 123.27 (2 CH of Ar), 127.51 (CH of Ar), 128.23 (2 CH of Ar), 129.28 (2 CH of Ar), 130.23 (2 CH of Ar), 138.48 (C<sub>ipso</sub>-CH), 139.67 (C<sub>ipso</sub>-C=O), 149.04 (C<sub>ipso</sub>-NO<sub>2</sub>), 164.61 (C=O), 168.38 ppm (C=O). MS (EI, 70 eV): m/z (%) = 382 (M<sup>+</sup> + 1, 1), 314 (4), 256 (100), 208 (5), 150 (34), 120 (8), 104 (20), 76 (13), 55 (10), 41 (5). Anal. calcd. for C<sub>21</sub>H<sub>23</sub>N<sub>3</sub>O<sub>4</sub> (381.43): C, 66.13; H, 6.08; N, 11.02%. Found: C, 66.14; H, 6.09; N, 11.04%.

#### $N^1$ -[2-(tert-Butylamino)-2-oxo-1-phenylethyl]-2-furamide (3i)

Yield: 0.29 g (96%); white crystals; mp = 174–176 °C. IR (KBr): 3334 (NH), 1640 (C=O), 1553 and 1475 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, DMSO- $d_6$ ):  $\delta_H$  = 1.20 (9 H, s,  $Me_3$ C), 5.61 (1 H, d,  $^3J_{\rm HH}$  = 8.2 Hz, CH), 6.39 (1 H, s, NH), 6.62 (1 H, d,  $^3J_{\rm HH}$  = 5.5 Hz, CH of furyl), 7.26 (1 H, t,  $^3J_{\rm HH}$  = 7.3 Hz, CH of Ar), 7.32 (2 H, t,  $^3J_{\rm HH}$  = 7.6 Hz, 2 CH of Ar), 7.42 (2 H, d,  $^3J_{\rm HH}$  = 7.5 Hz, 2 CH of Ar), 7.52 (1 H, s, CH of furyl), 7.84 (1 H, s, CH of furyl), 8.25 ppm (1 H, d,  $^3J_{\rm HH}$  = 7.6 Hz, NH). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_C$  = 28.26 ( $Me_3$ C), 50.46 ( $Me_3$ C), 55.7 (CH), 110.69 (CH of furyl), 114.12 (CH of furyl), 126.87 (2 CH of Ar), 127.4 (CH of Ar), 128.24 (2 CH of Ar), 139.07 ( $C_{ipso}$ -CH), 142.62 ( $C_{ipso}$ -C=O), 145.35 (CH of furyl), 156.74

(C=O), 168.68 ppm (C=O). MS (EI, 70 eV): m/z (%) = 236 (15), 450 (23), 183 (10), 112 (21), 95 (68), 71 (65), 57 (100), 43 (97). Anal. calcd. for  $C_{17}H_{20}N_2O_3$  (300.35): C, 67.98; H, 6.71; N, 9.33%. Found: C, 67.99; H, 6.72; N, 9.34%.

#### $N^2$ -[2-(Cyclohexylamino)-2-oxo-1-phenylethyl]-2-furamide (3j)

Yield: 0.32 g (98%); white crystals; mp = 154–156 °C. IR (KBr): 3260 (NH), 1671 and 1631 (C=O), 1553 and 1473 cm<sup>-1</sup> (Ar). <sup>1</sup>H NMR (500.13 MHz, CDCl<sub>3</sub>):  $\delta_{\rm H}$  = 1.10–1.89 (10 H, m, 5 CH<sub>2</sub> of cyclohexyl), 3.75–3.77 (1 H, m, CH), 5.54 (1 H, d,  $^3J_{\rm HH}$  = 6.6 Hz, CH), 6.00 (1 H, br, NH), 6.47 (1 H, dd,  $^3J_{\rm HH}$  = 3.2 Hz,  $^3J_{\rm HH}$  = 1.6 Hz, CH of furyl), 7.07 (1 H, d,  $^3J_{\rm HH}$  = 3.4 Hz, CH of furyl), 7.29–7.34 (3 H, m, 3 CH of Ar), 7.45 (2 H, d,  $^3J_{\rm HH}$  = 8.7 Hz, 2 CH of Ar), 7.46 (1 H, d,  $^3J_{\rm HH}$  = 8.7 Hz, CH of furyl), 7.74 ppm (1 H, d,  $^3J_{\rm HH}$  = 6.4 Hz, NH). <sup>13</sup>C NMR (125.75 MHz, CDCl<sub>3</sub>):  $\delta_{\rm C}$  = 24.61 (CH<sub>2</sub>), 24.72 (CH<sub>2</sub>), 25.43 (CH<sub>2</sub>), 32.63 (CH<sub>2</sub>), 32.82 (CH<sub>2</sub>), 48.83 (CH), 56.77 (CH), 112.04 (CH of furyl), 114.58 (CH of furyl), 127.40 (2 CH of Ar), 128.37 (CH of Ar), 129.02 (2 CH of Ar), 138.26 ( $C_{ipso}$ -CH), 144.23 (CH of furyl), 147.68 ( $C_{ipso}$ -C=O), 157.66 (C=O), 168.64 ppm (C=O). MS (EI, 70 eV): m/z (%) = 313 (19), 285 (10), 264 (18), 236 (24), 201 (9), 95 (47), 71 (56), 57 (93), 43 (100). Anal. calcd. for C<sub>19</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub> (326.34): C, 69.92; H, 6.79; N, 8.58%. Found: C, 69.94; H, 6.80; N, 8.59%.

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