# Copper(II) Reagent-Promoted Degradation of *N*,*N*′-dialkyldiazenedicarboxamides

**Jun-ichi Yamaguchi,* Yukihito Murayama, and Takayuki Suyama***

Department of Applied Chemistry, Faculty of Engineering, Kanagawa Institute of Technology, Shimo-ogino, Atsugi, Kanagawa 243-0292

(Received August 17, 2001)

Degradation of *N*,*N*′-dialkyldiazenedicarboxamides with a copper(II) reagent, which was prepared from lithium 4-nitrophenoxide and copper(II) bromide in tetrahydrofuran, proceeded via formation of isocyanate to produce the corresponding 4-nitrophenyl *N*-alkylcarbamate with the evolution of nitrogen. Further, it was also found that 4-nitrophenyl *N*-alkylcarbamate reacted with primary or secondary amines to give the corresponding multisubstituted urea. Based on the above results, we developed a new method for the one-pot preparation of multisubstituted ureas from *N*,*N*′-dialkyldiazenedicarboxamides.

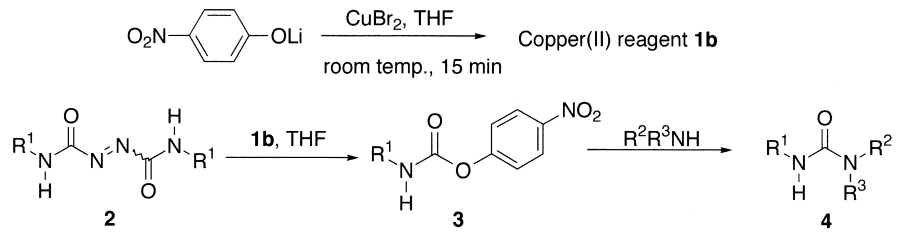
Previously, it was reported that a copper(II) reagent **1a** prepared from lithium *t*-butoxide and copper(II) bromide is useful for oxidative transformation of substrates containing a hydrogen–nitrogen bond. For example, oxidative transformation of amino groups,[1] hydrazine derivatives,[2] carboxamide,[3] *N*-substituted urea,[4] and *N*,*N*′-dialkyldiazenedicarboxamide[4] with **1a** afforded imines, gem-dihalo compounds, *t*-butyl ester, and *t*-butyl carbamate, respectively. Similarly, primary and secondary alcohols were oxidized with **1a** to the corresponding carbonyl compounds.[5]

Concerning the above transformation of functional groups using **1a**, we assume that *t*-butoxide is a strong base, so that **1a** can react with many types of functional groups.[1–5] Therefore, if a copper(II) reagent is prepared from aryloxide instead of *t*-butoxide, it will promote a chemoselective transformation. Transformation of functional groups is a basic task in organic synthesis, in which chemoselectivity is of special importance.

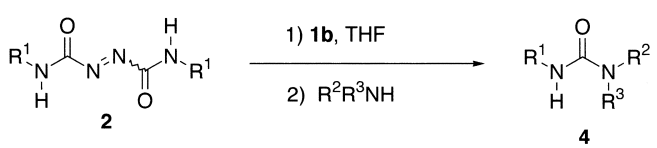
In the present study, we developed a new copper(II) reagent **1b** prepared from lithium 4-nitrophenoxide and copper(II) bromide, which transformed *N*,*N*′-dialkyldiazenedicarboxamides **2** chemoselectively into 4-nitrophenyl *N*-alkylcarbamates **3** with the evolution of nitrogen (Scheme 1). The reagent **1b** showed tolerance to primary and secondary amines, and *N*-substituted urea. We also report here the one-pot conversion of **2** into multisubstituted ureas **4** by treatment of the resulting carbamate **3** with amines (Scheme 2).

## Results and Discussion

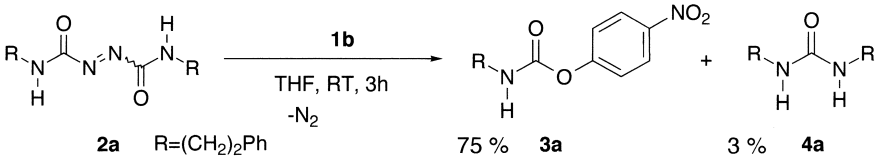
Initially, the preparation of several copper(II) reagents from lithium aryloxides and copper(II) bromide was examined. Since lithium 2-chlorophenoxide was brominated by treatment of copper(II) bromide to form 4-bromo-2-chlorophenol, the preparation of a copper(II) reagent from lithium 2-chlorophenoxide was unsuccessful. On the contrary, a copper(II) reagent **1b** prepared from lithium 4-nitrophenoxide and copper(II) bromide was stable in THF at room temperature.



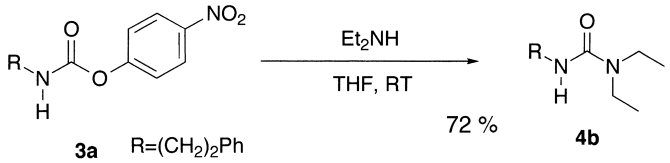

Scheme 1.




Scheme 2.




Scheme 3.




Scheme 4.

Next, we examined the oxidation of **2a** with **1b** in tetrahydrofuran (THF) at room temperature, and found that 4-nitrophenyl *N*-phenethylcarbamate **3a** and *N*,*N*′-diphenethylurea **4a** were produced in 75% and 3% yields, respectively (Scheme 3). The formation of **4a** is due to a small amount of water which existed in the reaction mixture. It is reasonable to assume that the reaction of phenethyl isocyanate with water affords phenethylamine and its addition to another isocyanate gives **4a**. 4-Nitrophenyl *N*-alkylcarbamate **3** as well as 4-nitrophenyl esters[6] and carbonates[7] are known as activated esters and react with primary or secondary amines to give the corresponding ureas.[8] It was found that the reaction of **3a** with diethylamine in THF gave *N*,*N*-diethyl-*N*′-phenethylurea **4b** in 72% yield (Scheme 4).

On the basis of these results, we next examined a one-pot preparation of multisubstituted ureas **4b** from **2a** (Table 1). Although the starting material **2a** was consumed when the reaction was performed at room temperature, the yield of **4b** was not satisfactory (Run 1). After several attempts, the yield of **4b** was improved when the reaction was performed at 50 °C, and the order of addition of reagents was changed (Run 4).

The one-pot preparation of **4** from various **2** and amines was carried out. The results listed in Table 2 show that the present reactions proceeded to give **4** in high yields in most cases. The yields apparently depend on the structures of **2** and the amine used. Unfortunately, the corresponding ureas **4** were obtained in low yield when an aromatic or a cyclic amine was employed (Runs 6 and 7).

Table 1. A One-Pot Preparation of *N*,*N*-Diethyl-*N*′-phenethylurea **4b**[a)]

| Run | Molar amounts of **1b** | Temperature | Time/min | Yield/% |
|---|---|---|---|---|
| 1 | 4.0 | RT | 15 | 54 |
| 2 | 2.1 | 50 °C | 15 | 58 |
| 3 | 3.2 | 50 °C | 15 | 75 |
| 4 | 4.0 | 50 °C | 15 | 87 |
| 5 | 5.2 | 50 °C | 15 | 66 |

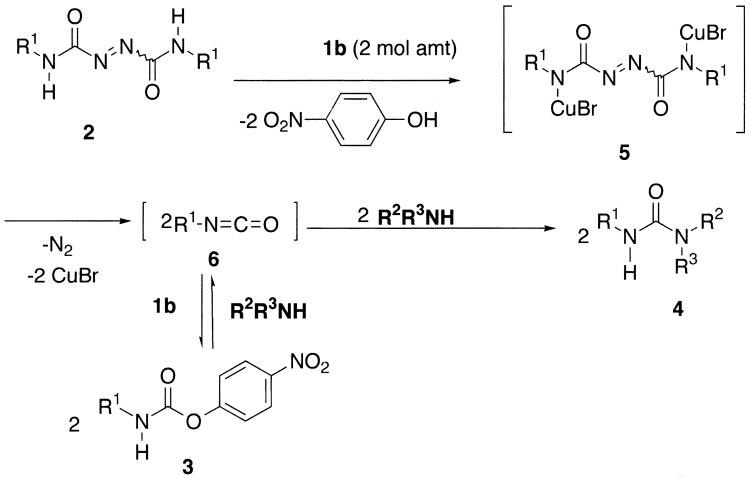
a) All reactions were carried out by method A except for Run 1. See experimental section.

The probable reaction mechanism of the one-pot preparation of multisubsituted ureas is outlined in Scheme 5. In the first step, the reaction of **2** with **1b** produces the copper(II) amide **5**, and the subsequent degradation of **5** gives isocyanate **6** with the evolution of nitrogen. Diels and Paquin have reported a similar pyrolysis of *N*,*N*′-diethyldiazenedicarboxamide

Table 2. The One-Pot Preparation of **4**[a)]

| Run | $R^1$ | | $R^2$ | $R^3$ | Method[b)] | Time/min | Compound | Yield/%[c)] |
|---|---|---|---|---|---|---|---|---|
| 1 | $Ph(CH_2)_2$ | **2a** | $PhCH_2$ | $PhCH_2$ | B | 15 | **4c** | 92 |
| 2 | | | *i*-Pr | *i*-Pr | A[d)] | 20 | **4d** | 84 |
| 3 | | | cyclohexyl | H | A[d)] | 20 | **4e** | 90 |
| 4 | | | *n*-Bu | H | A[d)] | 20 | **4f** | 86 |
| 5 | | | *t*-Bu | H | A[d)] | 20 | **4g** | 80 |
| 6[e)] | | | pyrrolidine | | A | 25 | **4h** | 49 |
| 7 | | | Ph | Me | A[d)] | 25 | **4i** | 34 |
| 8 | $PhCH_2$ | **2b** | $PhCH_2$ | $PhCH_2$ | A | 20 | **4j** | 66 |
| 9 | cyclohexyl | **2c** | $PhCH_2$ | $PhCH_2$ | A | 20 | **4k** | 86 |
| 10 | $Ph(CH_2)_3$ | **2d** | *n*-Bu | Me | A[d)] | 20 | **4l** | 80 |
| 11 | | | PhMeCH | H | A[d)] | 20 | **4m** | 90 |
| 12 | *n*-Bu | **2e** | $PhCH_2$ | $PhCH_2$ | B | 25 | **4n** | 83 |

a) All reactions were performed at 50 °C except for Run 6. b) See experimental section. c) Isolated yield of urea. d) Two molar amounts of amine were used. e) The reaction was carried out at room temperature.




Scheme 5.

bis-silver salt to form ethyl isocyanate.[9] Because *t*-butyl carbamate is produced by the addition of an alkoxycopper(II) species prepared from lithium *t*-butoxide and copper(II) bromide to isocyanate,[3] it is speculated that **1b** attacks isocyanate to afford 4-nitrophenyl carbamate **3**. Since alkaline hydrolysis[10] or aminolysis[11] of 4-nitrophenyl *N*-substituted carbamate affords the corresponding isocyanate, **6** will be regenerated by aminolysis of **3** under the present reaction conditions. In the last step, the addition of amine to **6** gives multisubstituted urea **4** as the final product.

In conclusion, we have found that the copper(II) reagent **1b** is powerful enough to promote the degradation of *N*,*N*′-dialkyldiazenedicarboxamides **2** to isocyanate **6**. This oxidative transformation can be used for preparation of multisubstituted ureas **4** from **2** and amines.

## Experimental

**General.** Melting points are uncorrected. IR spectra were measured on a JASCO FT/IR 410 spectrometer. $^1$H NMR spectra (300 MHz) and $^{13}$C NMR spectra (75 MHz) were recorded on a JEOL JMN-LA300 spectrometer using deuteriochloroform or DMSO-$d_6$ as a solvent with tetramethylsilane as an internal standard. Mass spectra were measured on a SHIMADZU GCMS-QP1000A spectrometer, and high resolution mass spectra were measured on a Hitachi M-80B spectrometer. Copper(II) halide was dried at 90–100 °C for several hours under reduced pressure.

**The Preparation of *N*,*N*′-Dialkyldiazenedicarboxamides 2.** The following compounds were prepared according to the reported method.[12]

***N*,*N*′-Diphenethyldiazenedicarboxamide (2a):** Orange crystals; mp 148–149 °C (decomp, EtOH);[4] IR (KBr) 3329, 1716 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 2.85 (t, $J$ = 7.1 Hz, 4H), 3.47 (td, $J$ = 7.1 and 5.4 Hz, 4H), 7.18–7.33 (m, 10H), 8.95 (brt, $J$ = 5.4 Hz, 2H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 35.09, 41.88, 126.36, 128.43, 128.70, 138.54, 161.19; Anal. Calcd for $C_{18}H_{20}N_4O_2$: C, 66.65; H, 6.21; N, 17.27%. Found: C 66.56, H 5.96, N 17.40%.

***N*,*N*′-Dibenzyldiazenedicarboxamide (2b):** Orange crystals; mp 188–189 °C (decomp, EtOH:DMF = 1:1 by volume); IR (KBr) 3238, 1709 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 4.44 (d, $J$ = 5.8 Hz, 4H), 7.27–7.38 (m, 10H), 9.38 (brt, $J$ = 5.8 Hz, 2H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 43.44, 127.19, 127.43, 128.39, 138.07, 161.82; Anal. Calcd for $C_{16}H_{16}N_4O_2$: C, 64.85; H, 5.44; N, 18.91%. Found: C 64.21, H 5.68, N 18.57%.

***N*,*N*′-Dicyclohexyldiazenedicarboxamide (2c):** Yellow crystals; mp 203–204 °C (decomp, EtOH);[4] IR (KBr) 3255, 2932, 2854, 1700 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.05–1.35 (m, 10H), 1.50–1.90 (m, 10H), 3.56 (brs, 2H), 8.80 (d, $J$ = 7.8 Hz, 2H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 24.40, 24.90, 31.94, 49.32, 160.63; Anal. Calcd for $C_{14}H_{24}N_4O_2$: C, 59.98; H, 8.63; N, 19.98%. Found: C 59.74, H 8.52, N 20.03%.

***N*,*N*′-Bis(3-phenylpropyl)diazenedicarboxamide (2d):** Orange crystals; mp 149.5–150.5 °C (decomp, EtOH); IR (KBr) 3235, 1707 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 1.96 (tt, $J$ = 7.3 and 7.3 Hz, 4H), 2.71 (t, $J$ = 7.3 Hz, 4H), 3.42 (q, $J$ = 7.3 Hz, 4H), 7.10–7.30 (m, 10H), 8.54 (brs, 2H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 30.69, 32.78, 39.98, 125.78, 128.25, 141.22, 161.49; Anal. Calcd for $C_{20}H_{24}N_4O_2$: C, 68.16; H, 6.86; N, 15.90%. Found: C 68.39, H 6.93, N 15.77%.

***N*,*N*′-Dibutyldiazenedicarboxamide (2e):** Orange crystals; mp 158 °C (decomp, EtOH); IR (KBr) 3263, 1707 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 0.94 (t, $J$ = 7.3 Hz, 6H), 1.39 (qt, $J$ = 7.3 and 7.3 Hz, 4H), 1.58 (tt, $J$ = 7.3 and 7.3 Hz, 4H), 3.31 (td, $J$ = 7.3 and 5.7 Hz, 4H), 8.69 (brt, $J$ = 5.7 Hz, 2H); $^{13}$C NMR (75 MHz, DMSO-$d_6$) $\delta$ 13.62, 19.74, 31.07, 40.10, 161.51; Anal. Calcd for $C_{10}H_{20}N_4O_2$: C, 52.61; H, 8.83; N, 24.54%. Found: C 52.43, H 8.59, N 24.79%.

**A Preparation of Lithium 4-Nitrophenoxide.** 4-Nitrophenol was added to a solution of an equimolar amount of lithium hydroxide monohydrate. After being stirred for several minutes, the reaction mixture was condensed under reduced pressure, followed by removal of a small amount of water as azeotrope using toluene. The residue was reprecipitated with THF and diethyl ether. The yellow precipitate was collected by filtration with suction, and then was dried at 140 °C for 5 h.

Orange crystals; mp > 300 °C; IR (KBr) 3613, 3581, 1587, 1329 cm$^{-1}$; $^1$H NMR (300 MHz, DMSO-$d_6$) $\delta$ 6.29 (d, $J$ = 7.3 Hz, 2H), 7.88 (d, $J$ = 7.3 Hz, 2H).

**Treatment of 2a with 1b.** To a THF solution (3.0 mL) of lithium 4-nitorophenoxide (218 mg, 1.50 mmol) was added copper(II) bromide (335 mg, 1.50 mmol) at room temperature under nitrogen, and the reaction mixture was stirred for 15 min. *N*,*N*′-Diphenethyldiazenedicarboxamide (**2a**) (81 mg, 0.25 mmol) was added to the reaction mixture. After the mixture had been stirred for 3 h, the reaction was quenched by addition of saturated $NH_4Cl$

solution (15 mL) and a small amount of 7.5% aqueous $NH_3$ solution. The organic materials were extracted with EtOAc (30 mL). The organic layer was washed with 0.25 M (1 M = 1 mol $dm^{-3}$) $Na_2CO_3$ solution (50 mL, 4 times) and water (50 mL, 5 times) successively, and was dried over $Na_2SO_4$. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (silica gel, hexane:EtOAc = 4:1) and **3a** (108 mg) and *N*,*N*′-diphenethylurea **4a** (4 mg) were obtained in 75% and 3% yields, respectively.

**4-Nitrophenyl Phenethylcarbamate (3a):** Mp 104–105 °C; IR (KBr) 3348, 1710, 1542 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 2.91 (t, $J$ = 6.8 Hz, 2H), 3.57 (q, $J$ = 6.8 Hz, 2H), 5.15 (brs, 1H), 7.22–7.35 (m, 7H), 8.23 (d, $J$ = 9.3 Hz, 2H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 35.71, 42.35, 121.88, 125.04, 126.73, 128.72, 128.73, 138.13, 144.65, 153.00, 155.86; MS (EI) *m*/*z* 147 ($Ph(CH_2)_2NCO^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{15}H_{14}N_2O$ 286.0953, found 286.0986.

***N*,*N*′-Diphenethylurea (4a):** Mp 110–111 °C; IR (KBr) 3427, 1655 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 2.83 (t, $J$ = 6.8 Hz, 4H), 3.45 (t, $J$ = 6.8 Hz, 4H), 4.62 (brs, 2H), 7.19–7.34 (m, 10H) ; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 36.14, 41.79, 126.52, 128.66, 128.84, 138.93, 158.23; MS (EI) *m*/*z* 164 ($M^+-C_8H_8$), 103 ($C_8H_8^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{17}H_{20}N_2O$ 268.1575, found 268.1608.

**One-Pot Preparations of Multisubstituted Ureas 4.** Method A: to a THF solution (4.0 mL) of lithium 4-nitorophenoxide (117 mg, 0.80 mmol) was added copper(II) bromide (179 mg, 0.80 mmol) at room temperature under nitrogen, and the reaction mixture was stirred for 15 min. After the resulting black solution was heated to 50 °C, amine (0.40 mmol), and subsequently **2** (0.20 mmol) was added to the solution. The reaction was quenched by addition of saturated $NH_4Cl$ solution (15 mL) and a small amount of 7.5% $NH_3$ solution. The organic materials were extracted with EtOAc (30 mL). The organic layer was washed with 0.25 M $Na_2CO_3$ solution (50 mL, 4 times) and water (50 mL, 5 times) successively, and was dried over $Na_2SO_4$. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (silica gel, $CHCl_3$:MeOH = 9:1 by volume) and urea **4** was isolated. Method B: to a THF solution (4.0 mL) of lithium 4-nitorophenoxide (117 mg, 0.80 mmol) was added copper(II) bromide (179 mg, 0.80 mmol) at room temperature under nitrogen, and the reaction mixture was stirred for 15 min. After the resulting black solution was heated to 50 °C, **2** (0.20 mmol) and subsequently amine (0.40 mmol) was added to the solution. The reaction was quenched by addition of saturated $NH_4Cl$ solution (15 mL) and a small amount of 7.5% aqueous $NH_3$ solution. The work-up and purification described as above gave urea **4**.

***N*,*N*-Diethyl-*N*′-phenethylurea (4b):** Oil; IR (neat) 3349, 1626, 1534 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.06 (t, $J$ = 7.1 Hz, 6H), 2.83 (t, $J$ = 6.8 Hz, 2H), 3.19 (q, $J$ = 7.1 Hz, 4H), 3.49 (q, $J$ = 6.8 Hz, 2H), 4.31 (brs, 1H), 7.19–7.33 (m, 5H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 13.72, 36.36, 41.26, 42.00, 126.33, 128.55, 128.88, 139.54, 157.12; MS (EI) *m*/*z* 220 ($M^+$), 100 ($C_5H_{10}NO^+$); HRMS (EI): calcd for $C_{13}H_{20}N_2O$ 220.1575, found 220.1579.

***N*,*N*-Dibenzyl-*N*′-phenethylurea (4c):** Mp 100.5–102.5 °C; IR (KBr) 3357, 1610, 1537 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 2.73 (t, $J$ = 6.8 Hz, 2H), 3.48 (q, $J$ = 6.8 Hz, 2H), 4.42 (s, 5H), 7.01–7.33 (m, 15H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 36.27, 42.09, 50.25, 126.24, 127.17, 127.42, 128.51, 128.73, 128.77, 137.57, 139.20, 158.38; MS (EI) *m*/*z* 344 ($M^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{23}H_{24}N_2O$ 344.1889, found 344.1937.

***N*,*N*-Diisopropyl-*N*′-phenethylurea (4d):** Mp 77–79 °C; IR (KBr) 3359, 1619, 1536 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.15 (d, $J$ = 6.8 Hz, 12H), 2.85 (t, $J$ = 6.8 Hz, 2H), 3.51 (q, $J$ = 6.8 Hz, 2H), 3.82 (sept, $J$ = 6.8 Hz, 2H), 4.14 (brs, 1H), 7.19–7.33 (m, 5H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 21.24, 36.13, 41.73, 44.82, 126.30, 128.50, 128.88, 139.61, 157.14; MS (EI) *m*/*z* 248 ($M^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{15}H_{24}N_2O$ 248.1889, found 248.1929.

***N*-Cyclohexyl-*N*′-phenethylurea (4e):** Mp 117.5–119 °C; IR (KBr) 2930, 2853, 1627, 1580 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.99–1.18 (m, 5H), 1.56–1.71 (m, 3H), 1.86–1.90 (m, 2H), 2.81 (t, $J$ = 6.8 Hz, 2H), 3.40–3.48 (m, 3H), 4.15 (brs, 1H), 4.26 (brs, 1H), 7.18–7.33 (m, 5H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 24.93, 25.59, 33.91, 36.40, 41.69, 49.20, 77.23, 126.43, 128.60, 128.86, 139.25, 157.39; MS (EI) *m*/*z* 246 ($M^+$), 83 ($C_6H_{11}^+$), 56 ($C_4H_8^+$); HRMS (EI): calcd for $C_{15}H_{22}N_2O$ 246.1732, found 246.1766.

***N*-Butyl-*N*′-phenethylurea (4f):** Mp 70–71 °C; IR (KBr) 3344, 1619, 1577 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.90 (t, $J$ = 7.1 Hz, 3H), 1.23–1.48 (m, 4H), 2.79 (t, $J$ = 6.8 Hz, 2H), 3.10 (q, $J$ = 7.1 Hz, 2H), 3.42 (q, $J$ = 6.8 Hz, 2H), 4.49 (brs, 1H), 4.54 (brs, 1H), 7.17–7.32 (m, 5H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 13.79, 20.02, 32.31, 36.47, 40.24, 41.66, 126.38, 128.56, 128.82, 139.26, 158.26; MS (EI) *m*/*z* 220 ($M^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{13}H_{20}N_2O$ 220.1575, found 220.1604.

***N*-*t*-Butyl-*N*′-phenethylurea (4g):** Mp 70–71 °C; IR (KBr) 3355, 1632, 1573 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.29 (s, 9H), 2.78 (t, $J$ = 6.8 Hz, 2H), 3.37 (t, $J$ = 6.8 Hz, 2H), 4.21 (brs, 2H), 7.17–7.31 (m, 5H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 29.55, 36.57, 41.48, 50.18, 126.30, 128.53, 128.82, 139.39, 157.75; MS (EI) *m*/*z* 220 ($M^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{13}H_{20}N_2O$ 220.1575, found 220.1590.

***N*-Phenethyl-1-pyrrolidinecarboxamide (4h):** Mp 84–85 °C; IR (neat) 3332, 1631, 1538 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.84–1.90 (m, 4H), 2.83 (t, $J$ = 7.1 Hz, 2H), 3.24–3.29 (m, 4H), 3.50 (t, $J$ = 7.1 Hz, 2H), 4.22 (brs, 1H), 7.19–7.33 (m, 5H) ; $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 25.54, 36.63, 41.80, 45.10, 126.31, 128.54, 128.85, 139.51, 156.76; MS (EI) *m*/*z* 218 ($M^+$), 98 ($C_5H_8NO^+$); HRMS (EI): calcd for $C_{13}H_{18}N_2O$ 218.1419, found 218.1436.

***N*-Methyl-*N*′-phenethyl-*N*-phenylurea (4i):** Oil; IR (neat) 1652, 1518 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 2.74 (t, $J$ = 7.1 Hz, 2H), 3.22 (s, 3H), 3.43 (t, $J$ = 7.1 Hz, 2H), 4.32 (brs, 1H), 7.07–7.37 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 36.26, 37.05, 42.00, 126.24, 127.20, 127.30, 128.46, 128.77, 129.91, 139.27, 143.29, 157.13; MS (EI) *m*/*z* 254 ($M^+$), 134 ($C_8H_8NO^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{16}H_{18}N_2O$ 254.1419, found 254.1473.

***N*,*N*-Dibenzyl-*N*′-cyclohexylurea (4j):** Mp 138.5–139.5 °C; IR (KBr) 3319, 2932, 1607, 1546 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.89–1.04 (m, 3H), 1.25–1.33 (m, 2H), 1.51–1.54 (m, 3H), 1.81–1.84 (m, 2H), 3.66–3.72 (m, 1H), 4.22 (d, $J$ = 7.5 Hz, 1H), 4.47 (s, 4H), 7.22–7.35 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 24.72, 25.57, 33.62, 49.33, 50.35, 127.27, 127.42, 128.74, 137.84, 157.79; MS (EI) *m*/*z* 322 ($M^+$), 106 ($C_7H_8N^+$), 91 ($C_7H_7^+$); HRMS (EI): calcd for $C_{21}H_{26}N_2O$ 322.2045, found 322.2058.

***N*,*N*,*N*′-Tribenzylurea (4k):** Mp 115.5–117 °C (lit.[13] 119–120 °C); IR (KBr) 3353, 1620, 1537 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 4.42 (d, $J$ = 5.6 Hz, 2H), 4.52 (s, 4H), 4.71 (brt, $J$ = 5.6 Hz, 1H), 7.09–7.36 (m, 15H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 44.95, 50.34, 127.05, 128.22, 127.47, 128.45, 128.78, 137.52, 139.33, 158.32; MS (EI) *m*/*z* 330 ($M^+$).

***N*-Butyl-*N*-methyl-*N′*-(3-phenylpropyl)urea (4l):** Oil; IR (neat) 3343, 2929, 1628, 1539 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.92 (t, $J$ = 7.3 Hz, 3H), 1.29 (tq, $J$ = 7.3 and 7.3 Hz, 2H), 1.44 (tq, $J$ = 7.3 and 7.3 Hz, 2H), 1.85 (tt, $J$ = 7.3 and 7.3 Hz, 2H), 2.66 (t, $J$ = 7.3 Hz, 2H), 2.77 (s, 3H), 3.18 (t, $J$ = 7.3 Hz, 2H), 3.28 (q, $J$ = 7.3 Hz, 2H), 4.37 (brs, 1H), 7.14–7.29 (m, 5H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 13.79, 19.94, 30.09, 31.85, 33.43, 33.99, 40.58, 48.41, 125.74, 128.27, 128.30, 141.83, 157.92; MS (EI) *m/z* 248 ($M^+$), 91 ($C_7H_7^+$), 57 ($C_4H_9^+$); HRMS (EI): calcd for $C_{15}H_{24}N_2O$ 248.1889, found 248.1903.

***N*-(1-Phenylethyl)-*N′*-(3-phenylpropyl)urea (4m):** Oil; IR (neat) 3333, 1631, 1568 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 1.42 (d, $J$ = 7.1 Hz, 3H), 1.71 (tt, $J$ = 7.8 and 7.8 Hz, 2H), 2.50 (t, $J$ = 7.8 Hz, 2H), 3.12 (dt, $J$ = 7.8 Hz, 2H), 4.48 (brs, 1H), 4.72 (dq, $J$ = 7.1 Hz, 1H), 4.85 (brd, $J$ = 7.1 Hz, 1H), 7.07–7.33 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 23.52, 31.72, 33.02, 39.90, 50.36, 125.86, 127.35, 128.33, 128.39, 128.77, 141,56, 144.19, 157.72; MS (EI) *m/z* 282 ($M^+$), 106 ($C_8H_{10}^+$); HRMS (EI): calcd for $C_{18}H_{22}N_2O$ 282.1732, found 282.1741.

***N*,*N*-Dibenzyl-*N′*-butylurea (4n):** Mp 86–87 °C; IR (neat) 3353, 2957, 2871, 1625, 1539 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 0.83 (t, $J$ = 7.3 Hz, 3H), 1.16 (tq, $J$ = 7.3 and 7.3 Hz, 2H), 1.36 (tt, $J$ = 7.3 and 7.3 Hz, 2H), 3.20 (q, $J$ = 7.3 Hz, 2H), 4.41 (brs, 1H), 4.48 (brs, 4H), 7.22–7.36 (m, 10H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 13.74, 19.88, 32.18, 40.68, 50.30, 127.21, 127.41, 128.75, 137.77, 158.55; MS (EI) *m/z* 296 ($M^+$), 106 ($C_7H_8N^+$); HRMS (EI): calcd for $C_{19}H_{24}N_2O$ 296.1889, found 296.1909.

## References


1 Oxidation of amino group: J. Yamaguchi and T. Takeda, *Chem. Lett*., **1992**, 1933. Oxidation of amino acid: T. Takeda, S. Yamauchi, and T. Fujiwara, *Synthesis*, **1996**, 600.

2 Oxidation of hydrazone: T. Takeda, R. Sasaki, A. Nakamura, S. Yamauchi, and T. Fujiwara, *Synlett*, **1996**, 273; T. Takeda, R. Sasaki, S. Yamauchi, and T. Fujiwara, *Tetrahedron*, **53**, 557 (1997). Oxidation of hydrazide; J. Yamaguchi, T.Aoyagi, R. Fujikura, and T. Suyama, *Chem. Lett*., **2001**, 466.

3 J. Yamaguchi, K. Hoshi, and T. Takeda, *Chem. Lett*., **1993**, 1273.

4 J. Yamaguchi, T. Shusa, and T. Suyama, *Tetrahedron Lett*., **40**, 8251 (1999).

5 J. Yamaguchi, S. Yamamoto, and T. Takeda, *Chem. Lett*., **1992**, 1185.

6 M. Bodanszky, *Nature*, **175**, 685 (1955); M. Bodanszky and V. du Vigneaud, *J. Am. Chem. Soc*., **81**, 5688 (1959).

7 K. Hoste, D. Bruneel, A. D. Marre, F. D. Schrijver, and E. Schacht, *Macromol. Rapid Commun*., **15**, 697 (1994); D. M. Dixit and C. C. Leznoff, *J. Chem. Soc., Chem. Commun*., **1977**, 798.

8 N. Choy, K. Y. Moon, C. Park, Y. C. Son, W. H. Jung, H.-i. Choy, C. S. Lee, C. R. Kim, and H. Yoon, *Org. Prep. Proc*., **28**, 173 (1996); B. Raji, J. M. Kassir, and T. P. Kogan, *Bioorg. Med. Chem. Lett*., **8**, 3043 (1998); Q. Liu, N. W. Luedtke, and Y. Tor, *Tetrahedron Lett*., **42**, 1445 (2001).

9 O. Diels and M. Paquin, *Ber. Dtsch. Chem. Ges*., **46**, 2000 (1913).

10 H. L. Bender and R. B. Homer, *J. Org. Chem*., **30**, 3975 (1965).

11 F. M. Menger and L. E. Glass, *J. Org. Chem*., **39**, 2469 (1974).

12 E. E. Smissman and A. Makriyannis, *J. Org. Chem*., **38**, 1652 (1973).

13 H. Hammerich, *Ber. Dtsch. Chem. Ges*., **25**, 1819 (1892).