Synthesis of imides and benzoylureas by direct oxidation of *N*-methylenes of amides and benzylureas

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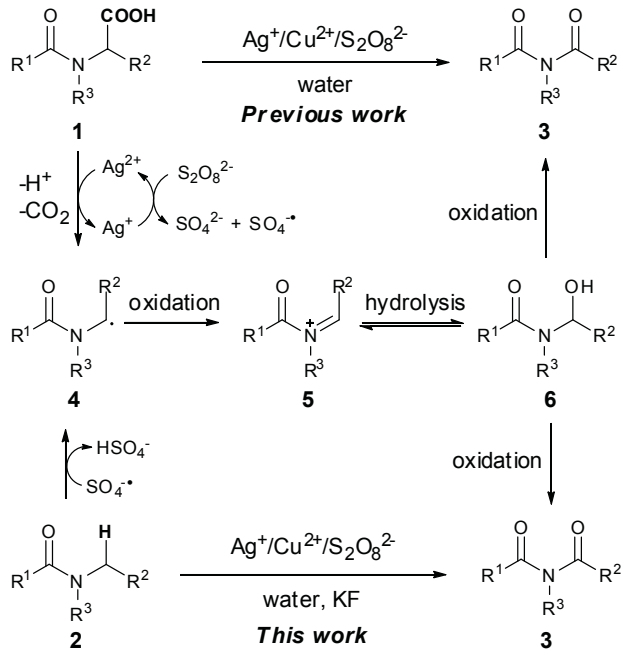
Some amides and benzylureas can be oxidised to imides and benzoylureas, respectively, using silver(I) nitrate (20 mol %), copper(II) sulfate pentahydrate (20 mol %), ammonium persulfate (3.0 equiv.), and potassium fluoride (20 equiv.) in water at room temperature.

Keywords: amide, benzylurea, direct oxidation, imide, benzoylurea, persulfate, potassium fluoride, silver(I) ion, copper(II) ion

The synthesis of imides by direct oxidation of amides attracts much attention in the context of mild reaction conditions compared with the traditional methods of acylation of amides. A number of oxidative systems have been developed, *e.g.* O_2/*N*-hydroxyphthalimide,[1] ruthenium porphyrin/pyridine-*N*-oxide,[2] chromium (VI)/periodic acid,[3] Dess–Martin periodinane,[4] and Selectfluor/CuBr.[5] However, these methods use either expensive reagents, or organic solvents or both, so new and simple methods are still needed. Here we report a mild method for direction oxidation of amides to imides using persulfate as the oxidative agent, with copper(II) and silver(I) catalysts, and water as solvent in the presence of an excess of KF.

Our previous work[6] demonstrated that *N*-acyl amino acids can be converted into imides by $S_2O_8^{2-}$/Ag^+/Cu^{2+}/water by oxidative decarboxylation followed by hydrolysis and further oxidation as shown at the top of Scheme 1. We speculated that replacing the carboxyl group with hydrogen may also form radical **4** through hydrogen abstraction by the sulfate anion radical, which would give imide **3** by the same path as from *N*-acyl amino acid, as shown at the bottom of Scheme 1. When we first examined the oxidation of amide **2a** under our previous standard conditions (20 mol % $AgNO_3$, 20 mol % $CuSO_4{\cdot}5H_2O$, 3.0 equiv. $(NH_4)_2S_2O_8$), we were delighted to observe the formation of the desired imide **3a** in 21% yield (Table 1, entry 1). After numerous trials, we found that in the presence of excess KF (20 equiv.), the yield of **3a** dramatically



Scheme 1

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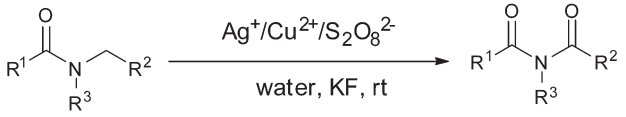
increased to 79%. Introducing a nitro group at the *para*-position of the benzoyl moiety of **2a** gave **3b** in 59% yield and **2c** with a *para*-methoxy group gave **3c** in 34% yield (Table 1, entries 3 and 4), indicating a profound effect of substitution on reaction efficiency. When we switched from benzoyl to aliphatic acyl, we were pleased to find that amide **2d** with an acetyl group afforded **3d** in the highest yield (83%) of these substrates tested, and the other three amides **2e–g** also smoothly underwent oxidation to give **3e–g** in 54–71% yields (Table 1, entries 5–8). This oxidation method was also effective for amide **2h** with a pyrrolidine ring replacing the 4-methoxybenzylamine of **2a** (Table 1, entry 9, 58% yield). Attempts to oxidise amides with a substituent such as Cl, Me and H, in place of the methoxy group of **2a** were unsuccessful.

Our protocol is not limited to amides. 1-Benzylurea **2i** can also be oxidised to 1-benzoylurea **3i** in 68% yield (Table 1, entry 10). 1-(4-Methylbenzyl)urea **2j** gave **3j** in a moderate yield whereas, 1-(4-methoxybenzyl)urea **2k** gave **3k** in a low yield (Table 1, entries 11 and 12). Surprisingly, 1-(4-methoxybenzyl)biuret **2l** also worked well, generating the desired 1-(4-methoxybenzoyl)biuret **3l** in a good yield (Table 1, entry 13, 79%). Although a number of methods have been developed for the direction oxidation of amides to imides, the direction oxidation of benzylurea to benzoylurea, to the best of our knowledge, has not been reported.

In summary, we have developed a new method to oxidise amides and benzylureas to imides and benzoylureas respectively. This represents the first example of direct oxidation of

Table 1 Synthesis of imides and benzoylureas by direct oxidation[a]



Entry	R^1	R^2	R^3	**2**	**3**	Yield/% of **3**
1	Ph	4-$MeOC_6H_4$	H	**2a**	**3a**	21[b]
2	Ph	4-$MeOC_6H_4$	H	**2a**	**3a**	79
3	4-$O_2NC_6H_4$	4-$MeOC_6H_4$	H	**2b**	**3b**	59[c]
4	4-$MeOC_6H_4$	4-$MeOC_6H_4$	H	**2c**	**3c**	34
5	Me	4-$MeOC_6H_4$	H	**2d**	**3d**	83
6	$MeOOCCH_2$	4-$MeOC_6H_4$	H	**2e**	**3e**	71
7	Bn	4-$MeOC_6H_4$	H	**2f**	**3f**	52
8	cyclohexyl	4-$MeOC_6H_4$	H	**2g**	**3g**	54[c]
9	Ph	$-(CH_2)_3-$		**2h**	**3h**	58[c]
10	H_2N	Ph	H	**2i**	**3i**	68
11	H_2N	4-MeC_6H_4	H	**2j**	**3j**	48[c]
12	H_2N	4-$MeOC_6H_4$	H	**2k**	**3k**	21
13	H_2NCONH	4-$MeOC_6H_4$	H	**2l**	**3l**	79

[a] Reaction conditions: $AgNO_3$ (20 mol %), $CuSO_4{\cdot}5H_2O$ (20 mol %), $(NH_4)_2S_2O_8$ (3.0 equiv.), and KF (20 equiv.) in water (10 mL), room temperature, 6 h except for those specified.
[b] In the absence of KF.
[c] These reactions were run overnight.

1-benzylurea to 1-benzoylurea. Our method features a cheap and bench-stable oxidant, water as a solvent and mild reaction conditions.

Experimental

Amide **2d**[7] and 1-benzylureas **2i–k**[8] were prepared according to the literature procedure. Compound **2l** was prepared from 1-nitrobiuret[9] and benzylamines according to the reported procedure.[10] ^{1}H and ^{13}C NMR spectra were recorded on a MercuPlus 400 NMR spectrometer. IR spectra were recorded on a Thermo Nicolet Avatar 360 IR spectrometer. Electrospray ionisation mass spectra were obtained on an LCQ Advantage MAX (Finnigan) instrument. All melting points were measured on a melting apparatus with microscope and hot stage and were uncorrected. Ammonium persulfate, $CuSO_4{\cdot}5H_2O$, and $AgNO_3$ were purchased from Jiangtian Chemical Reagent Company, China. These chemicals were used directly as received. The deionised water purchased from Water Centre of Nankai University, China, was distilled before use. All reactions were necessarily carried out under nitrogen. PE = petroleum ether (b.p. 60–90 °C).

Synthesis of amides **2a–c** *and* **2e–h***; general procedure*

CH_2Cl_2 (100 mL) was added to a flask (250 mL) containing a carboxylic acid (10 mmol) and HOBt (1.5 g, 11 mmol). After stirring at room temperature for 15 min under nitrogen, the mixture was cooled to 0 °C with ice-water bath and *N,N'*-dicyclohexylcarbodiimide (DCC) (2.3 g, 11 mmol) was added in portions. The reaction mixture was stirred for 15 min and then a solution of an amine (11 mmol) and triethylamine (1.0 g, 10 mmol) in CH_2Cl_2 (5 mL) was added dropwise over about 5 min. The reaction mixture was allowed to stir at 0 °C for 30 min and then at room temperature overnight. Then a solution of citric acid (10%, w/w, 100 mL) was added to decompose unreacted DCC, and the resulting mixture was stirred at room temperature for 1 h. The white solids (1,3-dicyclohexylurea) were washed with CH_2Cl_2 (5 mL × 2) after filtration. The combined filtrate was washed with citric acid solution (10%, w/w, 100 mL × 2), saturated Na_2CO_3 (100 mL × 2), and brine (50 mL), sequentially. The separated organic layer was dried over anhydrous Na_2SO_4, evaporated under reduced pressure, and the residue was purified by column chromatography (silica gel) or crystallisation using solvent as specified to give amides **2a–c** and **2e–h**.

N-*(4-Methoxybenzyl)benzamide* (**2a**): A white solid, yield 75%, m.p. 91–93 °C (lit.[11] 91–94 °C). IR (KBr, ν_{max}, cm^{-1}): 1634 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.73 (s, 3H, OCH_3), 4.44 (d, J = 5.6 Hz, 2H, NCH_2), 6.90 (d, J = 8.4 Hz, 2H, ArH), 7.28 (d, J = 8.4 Hz, 2H, ArH), 7.45–7.56 (m, 3H, ArH), 7.92 (d, J = 7.6 Hz, 2H, ArH), 9.02 (t, J = 5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 42.6, 55.5, 114.1, 127.7, 128.7, 129.1, 131.6, 132.1, 134.9, 158.7, 166.6. Crystallisation solvent: EtOAc: PE = 1: 5.

N-*(4-Methoxybenzyl)-4-nitrobenzamide* (**2b**): Yellow needles, yield 18%, m.p. 136–138 °C (lit.[12] 137–138.5 °C). IR (KBr, ν_{max}, cm^{-1}): 1641 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.73 (s, 3H, OCH_3), 4.44 (d, J = 6.0 Hz, 2H, NCH_2), 6.90 (d, J = 8.4 Hz, 2H, ArH), 7.27 (d, J = 8.4 Hz, 2H, ArH), 8.11 (d, J = 8.8 Hz, 2H, ArH), 8.32 (d, J = 8.8 Hz, 2H, ArH), 9.32 (t, J = 5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 42.8, 55.5, 114.2, 124.0, 129.20, 129.21, 131.5, 140.5, 149.5, 158.8, 164.9. Crystallisation solvent: absolute alcohol.

4-Methoxy-N-(4-methoxybenzyl)benzamide (**2c**): A white solid, yield 77%, m.p. 132–134 °C (lit.[12] 127–129 °C). IR (KBr, ν_{max}, cm^{-1}): 1632 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.73 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.42 (d, J = 5.2 Hz, 2H, NCH_2), 6.89 (d, J = 8.2 Hz, 2H, ArH), 7.01 (d, J = 8.4 Hz, 2H, ArH), 7.26 (d, J = 8.2 Hz, 2H, ArH), 7.90 (d, J = 8.4 Hz, 2H, ArH), 8.85 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 42.5, 55.5, 55.8, 113.9, 114.1, 127.2, 129.0, 129.5, 132.4, 158.6, 162.0, 166.1. Crystallisation solvent: EtOAc: PE = 1: 5.

Methyl 3-((4-methoxybenzyl)amino)-3-oxopropanoate (**2e**): A white solid, yield 13%, m.p. 71–73 °C. IR (KBr, ν_{max}, cm^{-1}): 1746 (C=O), 1643 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.30 (s, 2H, CH_2CONH), 3.63 (s, 3H, $COOCH_3$), 3.74 (s, 3H, $ArOCH_3$), 4.22 (d, J = 5.6 Hz, 2H, NCH_2), 6.89 (d, J = 8.6 Hz, 2H, ArH), 7.20 (d, J = 8.6 Hz, 2H, ArH), 8.53 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 42.2, 42.7, 52.3, 55.5, 114.2, 129.0, 131.4, 158.7, 165.5, 168.9. HRMS-ESI (negative): m/z [M+Na]$^+$ calcd for $C_{12}H_{15}NO_4Na^+$: 260.0893; found: 260.0897. Eluent: EtOAc: PE = 1: 1 (R_f = 0.32).

N-*(4-Methoxybenzyl)-2-phenylacetamide* (**2f**): A white solid, yield 43%, m.p. 142–144 °C (lit.[13] 142–144 °C). IR (KBr, ν_{max}, cm^{-1}): 1628 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.48 (s 2H, CH_2CO), 3.73 (s, 3H, OCH_3), 4.21 (d, J = 5.6 Hz, 2H, NCH_2), 6.87 (d, J = 8.4 Hz, 2H, ArH), 7.17 (d, J = 8.4 Hz, 2H, ArH), 7.21–7.31 (m, 5H, ArH), 8.50 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 42.2, 42.9, 55.5, 114.1, 126.8, 128.7, 129.0, 129.5, 131.8, 136.9, 158.7, 170.5. Crystallisation solvent: EtOAc: PE = 1: 5.

N-*(4-Methoxybenzyl)cyclohexanecarboxamide* (**2g**): A white solid, yield 17%, m.p. 119–121 °C (lit.[14] 118 °C). IR (KBr, ν_{max}, cm^{-1}): 1634 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.13–1.27 (m, 3H, cyclohexyl-H), 1.33–1.42 (m, 2H, cyclohexyl-H), 1.61–1.64 (m, 1H, cyclohexyl-H), 1.70–1.73 (m, 4H, cyclohexyl-H), 2.12–2.19 (m, 1H, CHC=O), 3.73 (s, 3H, OCH_3), 4.19 (d, J = 6.0 Hz, 2H, NCH_2), 6.87 (d, J = 8.6 Hz, 2H, ArH), 7.15 (d, J = 8.6 Hz, 2H, ArH), 8.12 (t, J = 5.6 Hz, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.8, 26.0, 29.8, 41.7, 44.5, 55.5, 114.1, 128.7, 132.3, 158.6, 175.5. Eluent: EtOAc: PE = 1: 3 (R_f = 0.29).

Phenyl(pyrrolidin-1-yl)methanone (**2h**): A colourless oil (mp: lit.[15] 46–47 °C), yield 20%. IR (KBr, ν_{max}, cm^{-1}): 1625 (C=O). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.73–1.79 (m, 2H, pyrrole-CH_2), 1.81–1.86 (m, 2H, pyrrole-CH_2), 3.31 (t, J = 7.0 Hz, 2H, pyrrole-CH_2), 3.54 (t, J = 7.0 Hz, 2H, pyrrole-CH_2), 7.28–7.30 (m, 3H, ArH), 7.40–7.44 (m, 2H, ArH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 26.3, 46.1, 49.5, 127.0, 128.1, 129.7, 137.2, 169.6. Eluent: EtOAc: PE = 1: 3 (R_f = 0.13).

Oxidation of amides and benzylureas; general procedure

$AgNO_3$ (13.6 mg, 0.08 mmol), $CuSO_4{\cdot}5H_2O$ (powder, 20.0 mg, 0.08 mmol), 1-benzylurea or amide (0.4 mmol), and $(NH_4)S_2O_8$ (273.8 mg, 1.2 mmol) were added to a plastic tube (25 mL). Then a solution of KF in water (0.8 M, 10 mL), which was degassed by purging with N_2 before use, was added by syringe. After stirring at room temperature for 6 h or overnight, the reaction mixture was treated with EtOAc (10 mL), and was allowed to stir for 5 min. The organic layer was separated, and the aqueous layer was extracted with EtOAc (10 mL × 2). The combined extracts were dried over anhydrous Na_2SO_4, evaporated, and separated by preparative TLC to give the product **3a–k**. For **2l**, after reaction, the reaction mixture was directly filtered, and the brown solids were washed with water (5 mL × 4) and EtOAc (5 mL x 4), sequentially, and then dried under reduced pressure to give the product **3l**.

N-*Benzoyl-4-methoxybenzamide* (**3a**): A pale yellow solid, yield 79%, m.p. 103–105 °C (lit.[16] 109–110 °C). IR (KBr, ν_{max}, cm^{-1}): 1719 and 1665 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.85 (s, 3H, OCH_3), 7.06 (d, J = 8.8 Hz, 2H, ArH), 7.50–7.55 (m, 2H, ArH), 7.61–7.66 (m, 1H, ArH), 7.90 (d, J = 7.2 Hz, 2H, ArH), 7.94 (d, J = 8.8 Hz, 2H, ArH), 11.18 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.0, 114.1, 126.2, 128.8, 129.0, 131.4, 132.9, 134.6, 163.3, 167.2, 168.4. Eluent: EtOAc: PE = 1:2 (R_f = 0.22).

4-Methoxy-N-(4-nitrobenzoyl)benzamide (**3b**): A pale yellow solid, yield 59%, m.p. 182–184 °C. IR (KBr, ν_{max}, cm^{-1}): 1709 and 1671 (C=O). ^{1}H NMR (400 MHz, acetone-d_6) δ 3.92 (s, 3H, OCH_3), 7.07 (d, J = 8.6 Hz, 2H, ArH), 8.03 (d, J = 8.6 Hz, 2H, ArH), 8.14 (d, J = 8.8 Hz, 2H, ArH), 8.36 (d, J = 8.8 Hz, 2H, ArH), 10.52 (brs, 1H, NH). ^{13}C NMR (100 MHz, acetone-d_6) δ 55.1, 113.8, 123.3, 125.5, 129.6, 130.8, 140.6, 149.9, 163.7, 165.8, 166.9. HRMS-ESI (positive): m/z [M+Na]$^+$ calcd for $C_{15}H_{12}N_2NaO_5^+$: 323.0638; found: 323.0634. Eluent: acetone: PE = 1:1 (R_f = 0.76).

4-Methoxyl-N-(4-methoxybenzoyl)benzamide (**3c**): A white solid, yield 34%, m.p. 170–172 °C (known[17] compound but no m.p. has been reported). IR (KBr, ν_{max}, cm^{-1}): 1715 and 1670 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.85 (s, 6H, OCH_3), 7.06 (d, J = 8.2 Hz, 4H, ArH), 7.92 (d, J = 8.2 Hz, 4H, ArH), 11.00 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.0, 114.1, 126.5, 131.3, 163.2, 167.4. Eluent: EtOAc: PE = 1:1 (R_f = 0.31).

N-*Acetyl-4-methoxybenzamide* (**3d**): A white solid, yield 83%, m.p. 116–118 °C (lit.[18] 119–119.5 °C). IR (KBr, ν_{max}, cm^{-1}): 1715 and 1676 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.36 (s, 3H, $C(O)CH_3$), 3.83 (s, 3H, OCH_3), 7.03 (d, J = 8.8 Hz, 2H, ArH), 7.95 (d, J = 8.8 Hz, 2H, ArH), 10.87 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 26.0, 55.9, 114.2, 125.6, 131.0, 163.3, 166.1, 172.8. Eluent: EtOAc: PE = 1:3 (R_f = 0.15).

Methyl 3-(4-methoxybenzamido)-3-oxopropanoate (**3e**): A pale yellow solid, yield 71%, m.p. 153–154 °C (known[19] compound but no m.p. has been reported). IR (KBr, ν_{max}, cm^{-1}): 1740, 1701 and 1679

(C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.65 (s, 3H, C(O)OCH$_3$), 3.82 (s, 2H, OOCCH$_2$), 3.85 (s, 3H, ArOCH$_3$), 7.05 (d, J = 9.0 Hz, 2H, ArH), 7.95 (d, J = 9.0 Hz, 2H, ArH), 11.20 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 45.2, 52.4, 56.0, 114.3, 129.0, 131.2, 163.6, 166.2, 168.1, 168.6. HRMS-ESI (negative): m/z [M+Na]$^+$ calcd for $C_{12}H_{13}NO_5Na^+$: 274.0686; found: 274.0689. Eluent: EtOAc: PE = 1:3 (R_f = 0.11).

4-Methoxy-N-(2-phenylacetyl)benzamide (**3f**): A pale yellow solid, yield 52%, m.p. 118–121 °C (lit.[20] 162–164 °C). IR (KBr, ν_{max}, cm^{-1}): 1710 and 1678 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.84 (s, 3H, OCH$_3$), 4.07 (s, 2H, CH$_2$CO), 7.06 (d, J = 9.0 Hz, 2H, ArH), 7.24–7.34 (m, 5H, ArH), 7.96 (d, J = 9.0 Hz, 2H, ArH), 11.00 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 43.9, 56.0, 114.2, 125.7, 127.0, 128.7, 130.1, 131.1, 135.5, 163.4, 166.1, 173.0. Eluent: EtOAc: PE = 1:2 (R_f = 0.46).

N-*(Cyclohexanecarbonyl)-4-methoxybenzamide* (**3g**): A white solid, yield 54%, m.p. 124–126 °C. IR (KBr, ν_{max}, cm^{-1}): 1703 and 1674 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.13–1.40 (m, 5H, cyclohexyl-H), 1.62–1.87 (m, 5H, cyclohexyl-H), 2.85–2.93 (m, 1H, cyclohexyl-H), 3.84 (s, 3H, OCH$_3$), 7.03 (d, J = 8.8 Hz, 2H, ArH), 7.90 (d, J = 8.8 Hz, 2H, ArH), 10.64 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 25.6, 25.9, 29.2, 44.6, 55.9, 114.1, 126.1, 131.0, 163.2, 166.0, 177.4. HRMS-ESI (negative): m/z [M-H]$^-$ calcd for $C_{15}H_{18}NO_3^-$: 260.1292; found: 260.1299. Eluent: EtOAc: PE = 1:1 (R_f = 0.60).

1-Benzoylpyrrolidin-2-one (**3h**): A white solid, yield 58%, m.p. 91–92 °C (lit.[21] 90–91 °C). IR (KBr, ν_{max}, cm^{-1}): 1744 and 1664 (C=O). ^{1}H NMR (400 MHz, CDCl$_3$) δ 2.09–2.17 (m, 2H, pyrrole-H), 2.59 (t, J = 8.0 Hz, 2H, pyrrole-CH$_2$), 3.95 (t, J = 7.2 Hz, 2H, pyrrole-CH$_2$), 7.28–7.40 (m, 2H, ArH), 7.49–7.54 (m, 1H, ArH), 7.59–7.63 (m, 2H, ArH). ^{13}C NMR (100 MHz, CDCl$_3$) δ 17.6, 33.3, 46.5, 127.8, 128.9, 131.8, 134.4, 170.6, 174.5. Eluent: EtOAc: PE = 1:1 (R_f = 0.66).

N-*Carbamoylbenzamide* (**3i**): A white solid, yield 68%, m.p. 205–208 °C (lit.[22] 208–210 °C). IR (KBr, ν_{max}, cm^{-1}): 1703 and 1660 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.41 (brs, 1H, one proton of NH$_2$), 7.48–7.53 (m, 2H, ArH), 7.59–7.64 (m, 1H, ArH), 7.95–7.98 (m, 2H, ArH), 8.07 (brs, 1H, another proton of NH$_2$), 10.54 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 128.6, 128.9, 133.1, 133.2, 154.7, 168.6. Eluent: CH$_2$Cl$_2$: MeOH = 15:1 (R_f = 0.60).

N-*Carbamoyl-4-methylbenzamide* (**3j**): A white solid, yield 48%, m.p. 223–225 °C (lit.[23] 224–225 °C). IR (KBr, ν_{max}, cm^{-1}): 1695 and 1674 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.36 (s, 3H, CH$_3$), 7.30 (d, J = 7.8 Hz, 2H, ArH), 7.38 (brs, 1H, one proton of NH$_2$), 7.88 (d, J = 7.8 Hz, 2H, ArH), 8.09 (brs, 1H, another proton of NH$_2$), 10.46 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 21.5, 128.6, 129.5, 130.3, 143.5, 154.8, 168.4. Eluent: CH$_2$Cl$_2$: MeOH = 15:1 (R_f = 0.61).

N-*Carbamoyl-4-methoxybenzamide* (**3k**): A white solid, yield 21%, m.p. 214–216 °C (lit.[24] 215 °C). IR (KBr, ν_{max}, cm^{-1}): 1704 and 1665 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.83 (s, 3H, OCH$_3$), 7.03 (d, J = 8.8 Hz, 2H, ArH), 7.35 (brs, 1H, one proton of NH$_2$), 7.99 (d, J = 8.8 Hz, 2H, ArH), 8.11 (brs, 1H, another proton of NH$_2$), 10.39 (brs, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.0, 114.2, 125.1, 130.7, 154.9, 163.3, 167.8. Eluent: CH$_2$Cl$_2$: MeOH = 12:1 (R_f = 0.59).

N-*(Carbamoylcarbamoyl)-4-methoxybenzamide* (**3l**): A brown solid, yield 79%, m.p. 225–226 °C. IR (KBr, ν_{max}, cm^{-1}): 1752, 1719 and 1675 (C=O). ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.85 (s, 3H, OCH$_3$), 7.07 (d, J = 8.6 Hz, 2H, ArH), 7.44 (s, 2H, NH$_2$), 7.99 (d, J = 8.6 Hz, 2H, ArH), 10.41 (s, 1H, NH), 11.19 (s, 1H, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ 56.1, 114.4, 124.4, 131.0, 152.7, 153.6, 163.8, 167.8. HRMS-ESI (negative): m/z [M-H]$^-$ calcd for $C_{10}H_{10}N_3O_4^-$: 236.0677; found: 236.0676. Eluent: CH$_2$Cl$_2$: MeOH = 10:1 (R_f = 0.56).

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