Supporting Information

Copper Catalyzed Oxidative Coupling of Amines with Formamides: A New Approach for the Synthesis of Unsymmetrical Urea Derivatives

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1. General Information:

All chemicals were purchased from Sigma-Aldrich and S.D Fine Chemicals, AVRA chemicals Pvt. Ltd. India and used as received. ACME silica gel (100–200 mesh) was used for column chromatography and Thin layer chromatography (TLC) was carried out on TLC Silica gel 60 F₂₅₄ and compounds were visualized by UV light, I₂ vapors, phosphomolybdic acid stain, ninhydrin stain. All the other chemicals and solvents were obtained from commercial sources and purified using standard methods. The IR values are reported in reciprocal centimeters (cm⁻¹). All ¹H, ¹³C{¹H} NMR spectra were recorded on a Avance-300, Inova-400, Inova-500 MHz Spectrometer. Chemical shifts (δ) are reported in ppm, using TMS (δ =0) as an internal standard in CDCl₃. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; q, quintet; dd, doublet of doublet; dt, doublet of triplet. The coupling constants (J), are reported in Hertz (Hz). Mass spectral data were compiled using MS (ESI), HRMS mass spectrometers. HPLC data recorded on SHIMAZDU HPLC Instrument equipped with DIODE ARRAY detector; Mobile phase: methanol : water = 90% +10% (1.5% acetic acid in HPLC water); Flow rate: 0.5 ml/min.; Column: LUX5M AMYLOSE-2 (phenomenox); UV-range : 190 nm.
2. Optimization of reaction conditions: 

![Chemical Reaction Diagram](image)

<table>
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<th>entry</th>
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<td>4 h</td>
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\(^a\) Reaction conditions: 1a (1 equiv), catalyst (5 mol%), DMF 2a (2 mL, 27 equiv.), Oxidant (1.5 equiv.), r.t., 4 h. \(^b\) Isolated yields. \(^c\) 20 equivalents of DMF has taken in 2 mL of CH\(_3\)CN solvent and reaction time 1 h. \(^d\) 0.2 mL of pyridine was added as an additive.
2. Experimental section:

**General procedure for the synthesis of aliphatic urea derivatives** (Scheme 2, 3a-3v).

A solution of Amine (1a-l) (1.0 mmol), CuBr$_2$ (11 mg, 5 mol%) in 2 mL of the respective formamide (2a-d) was stirred at room temperature. To the same solution, a 5-6 M TBHP solution in decane (1.5 mmol) was added drop wise and stirred for 1hr. After completion of reaction time, formamide was either evaporated was removed under reduced pressure or directly proceeded for the conventional work up with ethyl acetate water mixture. The organic layer was separated and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent under reduced pressure afforded the crude product, which was purified by column chromatography on silica gel (hexane/ethyl acetate 4:6).

**General procedure for the synthesis of aromatic or hetero aromatic ureas** (Scheme 3, 5a-5f).

A solution of 2-carbonyl-substituted anilines (4a-f) (1.0 mmol), Cu(OTf)$_2$ (18 mg, 5 mol%) in 2 mL of dimethyl formamide 2a was stirred at room temperature. To the same solution, 5-6 M TBHP solution in decane (1.5 mmol) was added drop wise, temperature raised to 80$^\circ$C, and stirred for 3 h. After cooling to room temperature, the reaction mixture was extracted with ethyl acetate and dried over anhydrous Na$_2$SO$_4$. Removal of the solvent under reduced pressure afforded the crude product, which was purified by column chromatography on silica gel (hexane/ethyl acetate 8:2).
4. Spectroscopic data for the products:

![Chemical Structure](image)

**N, N-dimethyl-4-phenylpiperidine-1-carboxamide** : (scheme 2, entry 1, 3a)

Isolated yield = 65%; IR cm⁻¹: 2931, 1643, 1491, 1392, 1193, 1064, 904, 757, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.18 – 7.33 (m, 5H), 3.75 – 3.84 (m, 2H), 2.81 – 2.9 (m, 8H), 2.66 (tt, J = 3.7, 11.8 Hz, 1H), 1.82 – 1.91 (m, 2H), 1.63 – 1.76 (m, 2H). ¹³C NMR δ(75 MHz, CDCl₃): 165, 145.7, 128.3, 126.6, 126.2, 47.4, 42.8, 38.4, 33.1. MS (ESI): m/z = 233 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₄H₂₁N₂O (M+H)⁺ = 233.16484, found = 233.16449.

![Chemical Structure](image)

**1, 1, 3-trimethyl-3-phenylurea** : (scheme 2, entry 2, 3b)

Isolated yield = 52%; IR cm⁻¹: 2926, 1641, 1496, 1454, 1383, 1167, 1122, 747, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.28-7.3 (m, Ar, 2H), 7.18-7.24 (m, Ar, 3H), 3.4 (t, J = 7.5 Hz, 2H), 2.85 (t, J = 7.5 Hz, 2H), 2.81 (s, 3H), 2.74 (s, 6H). ¹³C NMR δ(75 MHz, CDCl₃): 165.1, 139.2, 128.5, 128.2, 126, 51.7, 38.4, 36.8, 33.9. MS (ESI): m/z = 207 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₂H₁₉N₂O (M+H)⁺ = 207.14919, found = 207.14900.

![Chemical Structure](image)

**4-benzyl-N, N-dimethylpiperidine-1-carboxamide** : (scheme 2, entry 3, 3c)

Isolated yield = 49%; IR cm⁻¹: 2922, 2848, 1643, 1493, 1449, 1393, 1059, 746, 701. ¹H NMR δ(300 MHz, CDCl₃) 7.28-7.34 (m, Ar, 2H), 7.12-7.21 (m, Ar, 3H), 3.61-3.66 (m, 2H), 2.8 (s, 6H), 2.62-2.72 (m, 2H), 2.54 (d, J = 6.7 Hz, 2H), 1.59-1.71 (m, 3H), 1.15-1.28 (m, 2H). ¹³C NMR δ (75 MHz,
CDCl3: 165, 140.1, 128.9, 125.7, 46.9, 43, 38.4, 38.2, 31.8. MS (ESI): m/z = 247 (M+H)^+. HRMS ESI (M+H)^+ m/z calcld for C_{15}H_{23}N_{2}O (M+H)^+ = 247.18049, found = 247.17982.

\[ \text{CDCl3:} \quad 165, 140.1, 128.9, 125.7, 46.9, 43, 38.4, 38.2, 31.8. \text{MS (ESI):} \quad m/z = 247 \text{ (M+H)}^+. \text{HRMS ESI (M+H)}^+ m/z \text{ calcld for C}_{15}\text{H}_{23}\text{N}_{2}\text{O (M+H)}^+ = 247.18049, \text{found = 247.17982.} \]

\[ \begin{array}{c}
\text{Scheme 2, entry 4, 3d)} \\
N,N, 4\text{-trimethylpiperidine-1-carboxamide :} \\
\text{Isolated yield = 36% ; IR cm}^{-1}: 2923, 1644, 1493, 1450, 1135, 1060, 970. \text{^1H NMR } \delta(300 \text{ MHz, CDCl}_3): 3.6-3.65 \text{ (m, 2H), 2.8 (s, 6H), 2.71 (td, } J = 2.4, 13 \text{ Hz, 2H), 1.6-1.65 (m, 2H), 1.44-1.54 \text{ (m, 1H), 1.14 (qd, } J = 3.9, 12.8 \text{ Hz, 2H), 0.94 (d, } J = 6.4 \text{ Hz, 3H).} \text{^13C NMR } \delta(75 \text{ MHz CDCl3):} \quad 165.1, 47, 38.4, 33.9, 31.1, 21.7. \text{MS (ESI):} \quad m/z = 171 \text{ (M+H)}^+. \text{HRMS ESI (M+H)}^+ m/z \text{ calcld for C}_{9}\text{H}_{19}\text{N}_{2}\text{O (M+H)}^+ = 171.14919, \text{found = 171.14894.} \]

\[ \begin{array}{c}
\text{1, 1-dibutyl-3,3-dimethylurea :} \\
\text{Isolated yield = 29% ; IR cm}^{-1}: 2957, 2929, 1648, 1498, 1382, 1200, 1138. \text{^1H NMR } \delta(300 \text{ MHz, CDCl}_3) \quad 3.09 \text{ (t, } J = 6.9 \text{ Hz, 4H), 2.76 (s, 6H), 1.46 (p, } J = 6.9 \text{ Hz, 4H), 1.22-1.3 \text{ (m, 4H), 0.89 (t, } J = 6.9 \text{ Hz, 6H).} \text{^13C NMR } \delta(75 \text{ MHz CDCl3):} \quad 165.5, 47.7, 38.6, 30, 20, 13.7. \text{MS (ESI):} \quad m/z = 201 \text{ (M+H)}^+. \text{HRMS ESI (M+H)}^+ m/z \text{ calcld for C}_{11}\text{H}_{25}\text{N}_{2}\text{O (M+H)}^+ = 201.19614, \text{found = 201.19582.} \]

\[ \begin{array}{c}
\text{N,N-dimethylpyrrolidine-1-carboxamide :} \\
\text{Isolated yield = 21% ; IR cm}^{-1}: 2930, 2873, 1632, 1453, 1387, 1347, 1064, 777. \text{^1H NMR } \delta(300 \text{ MHz, CDCl}_3): 3.3-3.37 \text{ (m, 4H), 2.83 (s, 6H), 1.79-1.84 (m, 4H).} \text{^13C NMR } \delta(75 \text{ MHz CDCl3):} \quad 163.5, 48.3, 38.1, 25.4. \text{MS (ESI):} \quad m/z = 143 \text{ (M+H)}^+. \text{HRMS ESI (M+H)}^+ m/z \text{ calcld for C}_{7}\text{H}_{15}\text{N}_{2}\text{O (M+H)}^+ = 143.11789, \text{found = 143.11758.} \]

\[ \begin{array}{c}
\text{N,N-dimethylpyrrolidine-1-carboxamide :} \\
\text{Isolated yield = 21% ; IR cm}^{-1}: 2930, 2873, 1632, 1453, 1387, 1347, 1064, 777. \text{^1H NMR } \delta(300 \text{ MHz, CDCl}_3): 3.3-3.37 \text{ (m, 4H), 2.83 (s, 6H), 1.79-1.84 (m, 4H).} \text{^13C NMR } \delta(75 \text{ MHz CDCl3):} \quad 163.5, 48.3, 38.1, 25.4. \text{MS (ESI):} \quad m/z = 143 \text{ (M+H)}^+. \text{HRMS ESI (M+H)}^+ m/z \text{ calcld for C}_{7}\text{H}_{15}\text{N}_{2}\text{O (M+H)}^+ = 143.11789, \text{found = 143.11758.} \]
N, N-dimethylmorpholine-4-carboxamide : (scheme 2, entry 7, 3g)
Isolated yield = 34%; IR cm⁻¹: 2854, 1643, 1494, 1392, 1203, 1115, 895. ¹H NMR δ(300 MHz, CDCl₃) 4.26 (m, 1H), 3.69 (t, J = 4.9 Hz, 4 H), 3.23 (t, J = 4.9 Hz, 4 H), 2.84 (s, 6H). ¹³C NMR δ (75 MHz, CDCl₃): 164.5, 66.4, 47, 38.1. MS (ESI): m/z = 159 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₇H₁₃N₂O₂ (M+H)⁺ = 159.11280, found = 159.11266.

N, N-dimethyl-4-phenylpiperidine-1-carboxamide : (scheme 2, entry 8, 3h)
Isolated yield = 63%; IR cm⁻¹: 2971, 2931, 1641, 1418, 1374, 1274, 1243, 755, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.3 (t, J = 6.9 Hz, 2H), 7.18-7.22 (m, Ar, 3H), 3.74-3.76 (m, 2H), 3.22 (q, J = 6.9 Hz, 4H), 2.85 (td, J = 2, 12.9 Hz, 2H), 2.65 (tt, J = 3.9, 11.9 Hz, 1H), 1.81-1.87 (m, 2H), 1.7 (qd, J = 3.9, 11.9 Hz, 2H), 1.13 (t, J = 6.9 Hz, 6H). ¹³C NMR δ(75 MHz, CDCl₃): 164.8, 145.8, 128.4, 126.7, 126.2, 47.8, 42.9, 41.7, 33.1, 13.2. MS (ESI): m/z = 261 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₆H₂₅N₂O (M+H)⁺ = 261.19614, found = 261.19571.

1,1-diethyl-3-methyl-3-phenethylurea : (scheme 2, entry 9, 3i)
Isolated yield = 58%; IR cm⁻¹: 2971, 2931, 1641, 1486, 1398, 1121, 983, 748, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.17-7.3 (m, Ar, 5H), 3.39 (t, J = 7.5 Hz, 2H), 3.1 (q, J = 6.9 Hz, 4H), 2.85 (t, J = 7.9 Hz, 2H), 2.81 (s, 3H), 1.06 (t, J = 6.9 Hz, 6H). ¹³C NMR δ(75 MHz, CDCl₃): 164.9, 139.4, 128.6, 128.3, 126.1, 52, 41.9, 37, 34, 13.1. MS (ESI): m/z = 235 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₄H₂₅N₂O (M+H)⁺ = 235.18049, found = 235.18019.
**4-benzyl-N, N-diethylpiperidine-1-carboxamide: (scheme 2, entry 10, 3j)**

Isolated yield = 53%; IR cm⁻¹: 2926, 1642, 1416, 1373, 1250, 964, 745, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.25-7.3 (m, Ar, 2H), 7.18-7.21 (m, Ar, 1H), 7.12-7.15 (m, Ar, 2H), 3.57-3.62 (m, 2H), 3.17 (q, J = 6.7 Hz, 4H), 2.66 (td, J = 2.2, 12.8 Hz, 2H), 2.54 (d, J = 6.7 Hz, 2H), 1.59-1.7 (m, 3H), 1.18-1.28 (m, 2H), 1.1 (t, J = 6.7 Hz, 6H). ¹³C NMR δ(75 MHz, CDCl₃): 164.7, 140.1, 128.9, 128.1, 125.7, 47.3, 43.1, 41.7, 38.3, 31.9, 13.1. MS (ESI): m/z = 275 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₇H₂₇N₂O (M+H)⁺ = 275.21179, found = 275.21118.

**Morpholino(4-phenylpiperidin-1-yl)methanone: (scheme 2, entry 11, 3k)**

Isolated yield = 41%; IR cm⁻¹: 2919, 2851, 1643, 1417, 1271, 1223, 1114, 1012, 757, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.28-7.33 (m, Ar, 2H), 7.18-7.23 (m, Ar, 3H), 3.81-3.87 (m, 2H), 3.7 (t, J = 4.5 Hz, 4H), 3.28 (t, J = 4.5 Hz, 4H), 2.89 (td, J = 2.4, 13 Hz, 2H), 2.67 (tt, J = 3.5, 11.8 Hz, 1H), 1.84-1.88 (m, 2H), 1.65-1.75 (m, 2H). ¹³C NMR δ(75 MHz CDCl₃): 163.9, 145.4, 128.3, 126.6, 126.2, 66.5, 47.3, 42.7, 33. MS (ESI): m/z = 275 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₆H₂₃N₂O₂ (M+H)⁺ = 275.17540, found = 275.17499.

**N-methyl-N-phenethylmorpholine-4-carboxamide: (scheme 2, entry 12, 3l)**

Isolated yield = 40%; IR cm⁻¹: 2923, 1643, 1489, 1453, 1395, 1115, 1068, 749, 701. ¹H NMR δ(300 MHz, CDCl₃) 7.27-7.31 (m, Ar, 2H), 7.18-7.23 (m, Ar, 3H), 3.6 (t, J = 4.9 Hz, 4H), 3.45 (t, J = 7.9 Hz, 2H), 3.11 (t, J = 4.9 Hz, 4H), 2.84-2.87 (m, 5H). ¹³C NMR δ(75 MHz, CDCl₃): 164.2, 139, 128.6, 128.3, 126.1, 66.4, 51.3, 47.1, 36.6, 33.7. MS (ESI): m/z = 249 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₄H₂₁N₂O₂ (M+H)⁺ = 249.15975, found = 249.15926.
1,1-dimethyl-3-(1-phenylethyl)urea : (scheme 2, entry 13, 3m)
Isolated yield = 49% ; IR cm⁻¹: 2929, 1630, 1528, 1377, 1226, 761, 700. ¹H NMR δ(300 MHz, CDCl₃) 7.29-7.34 (m, Ar, 4H), 7.21-7.25 (m, 1H), 5.01 (p, J = 6.9 Hz, 1H), 4.6 (bs, 1H), 2.89 (s, 6H), 1.48 (d, J = 6.7 Hz, 3H). ¹³C NMR δ (75 MHz, CDCl₃): 157.5, 144.4, 128.4, 126.9, 125.9, 49.9, 36, 22.5. MS (ESI): m/z = 193 (M+H)+. HRMS ESI (M+H)+ m/z calcd for C₁₁H₁₇N₂O (M+H)+ = 193.13354, found = 193.13336.

3-cyclohexyl-1, 1-dimethylurea : (scheme 2, entry 14, 3n)
Isolated yield = 56%; IR cm⁻¹: 2930, 1625, 1534, 1388, 1359, 1217, 1030. ¹H NMR δ(300 MHz, CDCl₃) 4.18 (bs, 1H), 3.56-3.69 (m, 1H), 2.88 (s, 6H), 1.92-1.97 (m, 2H), 1.62-1.73 (m, 4H), 1.29-1.44 (m, 2H), 1.02-1.2 (m, 2H). ¹³C NMR δ (75 MHz, CDCl₃): 157.7, 49.3, 36, 34, 25.6, 25. MS (ESI): m/z = 171 (M+H)+. HRMS ESI (M+H)+ m/z calcd for C₉H₁₉N₂O (M+H)+ = 171.14919, found = 171.14879.

3-cyclooctyl-1, 1-dimethylurea : (scheme 2, entry 15, 3o)
Isolated yield = 43%; IR cm⁻¹: 2921, 1634, 1522, 1340, 1327, 1201, 1021.¹H NMR δ(300 MHz, CDCl₃) 4.26 (m, 1H), 3.83-3.92 (m, 1H), 2.88 (s, 6H), 1.51-1.88 (m, 14H). ¹³C NMR δ (75 MHz, CDCl₃): 157.5, 50.3, 35.9, 32.9, 27, 25.3, 23.6. MS (ESI): m/z = 199 (M+H)+. HRMS ESI (M+H)+ m/z calcd for C₁₁H₂₃N₂O (M+H)+ = 199.18049, found = 199.18019.

N-(1-phenylethyl)morpholine-4-carboxamide : (scheme 2, entry 16, 3p)
Isolated yield = 33%; IR cm⁻¹: 2970, 2926, 1624, 1530, 1255, 1116, 995, 866, 762, 700, 564. ¹H NMR δ(300 MHz, CDCl₃) 7.32-7.37 (m, 4H), 7.22-7.29 (m, 1H), 5.02 (p, J = 6.7 Hz, 1H), 4.66 (bs, 1H), 3.67 (t, J = 4.7 Hz, 4H), 3.32-3.35 (m, 4H), 1.49 (d, J = 6.7 Hz, 3H). ¹³C NMR δ (75 MHz, CDCl₃): 156.9,
144.1, 128.4, 127, 125.9, 66.3, 49.9, 43.9, 22.4. MS (ESI): m/z = 235 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₃H₁₉N₂O₂ (M+H)⁺ = 235.14410, found = 235.14359.

**N-cyclohexylmorpholine-4-carboxamide**: (scheme 2, entry 17, 3q)

Isolated yield = 29%; IR cm⁻¹: 2929, 1614, 1538, 1454, 1414, 1274, 1252, 1109, 1074, 1027, 999, 855. ¹H NMR δ(300 MHz, CDCl₃) 4.26 (b, 1H), 3.62–3.69 (m, 5H), 3.31 (t, J = 4.9 Hz, 4H), 1.95 (dd, J = 3.9, 12.9 Hz, 2H), 1.68–1.77 (m, 2H), 1.59–1.63 (m, 1H), 1.32–1.41 (m, 2H), 1.05–1.19 (m, 3H). ¹³C NMR δ(75 MHz, CDCl₃): 157, 66.4, 49.3, 43.8, 33.8, 25.5, 24.9.

**Methyl 2-(3, 3-dimethylureido)-3-phenylpropanoate**: (scheme 2, entry 18, 3r)

Isolated yield = 39%; IR cm⁻¹: 2930, 1740, 1639, 1527, 1453, 1382, 1202, 746, 701. ¹H NMR δ(300 MHz, CDCl₃) 7.21–7.32 (m, 3H), 7.07–7.16 (m, 2H), 4.74–4.83 (m, 2H), 3.71 (s, 3H), 3.08–3.15 (m, 2H), 2.87 (bs, 6H). ¹³C NMR δ(75 MHz, CDCl₃): 173.1, 157.3, 136.2, 129.1, 128.3, 126.8, 54.3, 52, 38.3, 35.9. MS (ESI): m/z = 213 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₁H₂₁N₂O₂ (M+H)⁺ = 213.15975, found = 213.15929.

**Methyl 2-(3, 3-dimethylureido)-3-methylbutanoate**: (scheme 2, entry 19, 3s)

Isolated yield = 41%; IR cm⁻¹: 2937, 1744, 1632, 1502, 1435, 1352, 1242, 1085. ¹H NMR δ(300 MHz, CDCl₃) 4.85 (b, 1H), 4.42–4.46 (m, 1H), 3.73 (s, 3H), 2.94 (bs, 6H), 2.07–2.19 (m, 1H), 0.93 (q, J = 6.7 Hz, 6H). ¹³C NMR δ(75 MHz, CDCl₃): 173.8, 157.8, 58.3, 51.8, 36, 31.1, 18.8, 17.7. MS (ESI): m/z = 203 (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₉H₁₉N₂O₃ (M+H)⁺ = 203.13902, found = 203.13894.
N-methyl-4-phenylpiperidine-1-carboxamide : (scheme 2, entry 20, 3t)

Isolated yield = 48%; IR cm⁻¹: 2933, 1626, 1547, 1395, 1242, 1009, 756, 700. \(^1\)H NMR δ(300 MHz, CDCl₃) 7.28-7.33 (m, Ar, 2H), 7.18-7.23 (m, Ar, 3H), 4.6 (bs, 1H), 4.06-4.1 (m, 2H), 2.82-2.92 (m, 5H), 2.66 (tt, \(J = 3.5, 12\) Hz, 1H), 1.82-1.87 (m, 2H), 1.65 (qd, \(J = 3.9, 12.4\) Hz, 2H). \(^{13}\)C NMR δ (75 MHz, CDCl₃): 158.3, 145.4, 128.4, 126.6, 126.2, 44.5, 42.5, 32.9, 27.5. MS (ESI): \(m/z = 219\) (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₃H₁₉N₂O (M+H)⁺ = 219.14919, found = 219.14874.

4-benzyl-N-methylpiperidine-1-carboxamide : (scheme 2, entry 22, 3v)

Isolated yield = 52%; IR cm⁻¹: 2918, 1624, 1546, 1417, 1396, 1253, 1149, 1032, 961, 746, 700. \(^1\)H NMR δ(300 MHz, CDCl₃) 7.25-7.30 (m, Ar, 2H), 7.16-7.21 (m, Ar, 1H), 7.11-7.14 (m, Ar, 2H), 4.54 (bs, 1H), 3.87-3.92 (m, 2H), 2.78 (d, \(J = 3.7\) Hz, 3H), 2.69 (td, \(J = 2.2, 12.8\) Hz, 2H), 2.53 (d, \(J = 6.7\) Hz, 2H), 1.61-1.72 (m, 3H), 1.1-1.23 (m, 2H). \(^{13}\)C NMR δ(75 MHz, CDCl₃): 158.4, 139.9, 128.9, 128, 125.8, 44, 42.9, 37.9, 31.6, 27.4. MS (ESI): \(m/z = 233\) (M+H)⁺. HRMS ESI (M+H)⁺ m/z calcd for C₁₄H₂₁N₂O (M+H)⁺ = 233.16484, found = 233.16444.
3-(2-acetylyphenyl)-1, 1-dimethylurea : (scheme 3, entry 1, 5a)

Isolated yield = 31% ; IR cm$^{-1}$: 2927, 1677, 1644, 1586, 1530, 1362, 1242, 1180, 1163, 959, 758, 695. $^1$H NMR $\delta$(300 MHz, CDCl$_3$) 11.42 (bs, 1H), 8.65 (dd, $J = 0.7$, 8.4 Hz, 1H), 7.86 (dd, $J = 1.5$, 8.1 Hz, 1H), 7.51 (td, $J = 1.3$, 8.4 Hz, 1H), 6.99 (td, $J = 1.1$, 8.1 Hz), 3.09 (bs, 6H), 2.66 (s, 3H). $^{13}$C NMR $\delta$(75 MHz, CDCl$_3$): 202.8, 155.6, 143.2, 135, 131.5, 120.1, 119.5, 36.2, 29.5. MS (ESI): m/z = 229 (M+Na)$^+$. HRMS ESI (M+Na)$^+$ m/z calcd for C$_{11}$H$_{14}$N$_2$O$_2$Na (M+Na)$^+$ = 229.09475, found = 229.09441.

3-(2-benzoylphenyl)-1, 1-dimethylurea : (scheme 3, entry 2, 5b)

Isolated yield = 38% ; IR cm$^{-1}$: 2928, 1678, 1629, 1582, 1523, 1447, 1361, 1255, 1176, 938, 752, 700, 644. $^1$H NMR $\delta$(300 MHz, CDCl$_3$) 10.77 (bs, 1H), 8.56 (dd, $J = 1.1$, 8.6 Hz, 1H), 7.65 – 7.67 (m, 2H), 7.45 – 7.61 (m, 5H), 6.95 (td, $J = 1.1$, 8.1 Hz, 1H), 3.11 (bs, 6H). $^{13}$C NMR $\delta$ (75 MHz, CDCl$_3$): 200.3, 153.1, 139, 134.5, 133.9, 129.5, 128.1, 121.6, 120.3, 119.9, 36.2. MS (ESI): m/z = 269 (M+H)$^+$. HRMS ESI (M+H)$^+$ m/z calcd for C$_{16}$H$_{17}$N$_2$O$_2$ (M+H)$^+$ = 269.12845, found = 269.12799.

3-(2-benzoyl-4-chlorophenyl)-1, 1-dimethylurea : (scheme 3, entry 3, 5c)

Isolated yield = 39% ; IR cm$^{-1}$: 2929, 1677, 1634, 1578, 1512, 1397, 1362, 1240, 1175, 950, 832, 747, 701. $^1$H NMR $\delta$(300 MHz, CDCl$_3$) 10.6 (bs, 1H), 8.54 - 8.57 (m, 1H), 7.59 – 7.68 (m, 3H), 7.47 – 7.53 (m, 4H), 3.09 (bs, 6H). $^{13}$C NMR $\delta$ (75 MHz, CDCl$_3$): 199, 155.2, 141.6, 138.3, 134.2, 132.7, 129.5, 128.4, 124.9, 122.7, 122, 36.2. MS (ESI): m/z = 303 (M+H)$^+$. HRMS ESI (M+H)$^+$ m/z calcd for C$_{16}$H$_{16}$ClN$_2$O$_2$ (M+H)$^+$ = 303.08948, found = 303.08905.
3-(2-benzoyl-4-nitrophenyl)-1, 1-dimethylurea : (scheme 3, entry 4, 5d)

Isolated yield = 35\%; IR cm\(^{-1}\): 2925, 2854, 1694, 1623, 1508, 1252, 959, 750, 697, 553. \(^1\)H NMR \(\delta\)(300 MHz, CDCl\(_3\)) 11.21 (bs, 1H), 8.83 (d, \(J = 9\) Hz, 1H), 8.51 (d, \(J = 3\) Hz, 1H), 8.38 (dd, \(J = 9.8\) Hz, 1H), 7.64 – 7.69 (m, 3H), 7.55 (t, \(J = 6.7\) Hz, 2H), 3.15 (bs, 6H). \(^13\)C NMR \(\delta\)(75 MHz, CDCl\(_3\)): 199, 154.4, 148.6, 139.7, 137.8, 133, 129.6, 129.1, 128.7, 120.2, 120.1, 36.4. MS (ESI): m/z = 314 (M+H\(^+\)). HRMS ESI (M+H\(^+\)) \(m/z\) calcd for C\(_{16}\)H\(_{16}\)N\(_3\)O\(_4\) (M+H\(^+\)) = 314.11353, found = 314.11322.

Methyl 4-chloro-1-(dimethylcarbamoyl)-1\(H\)-indole-2-carboxylate : (scheme 3, entry 5, 5e)

Isolated yield = 37\%; IR cm\(^{-1}\): 2929, 1708, 1530, 1441, 1390, 1245, 1199, 1060, 763, 729. \(^1\)H NMR \(\delta\)(300 MHz, CDCl\(_3\)) 7.66 (bs, 1H), 7.32 – 7.34 (m, 1H), 7.24 – 7.27 (m, 2H), 4.38 (q, \(J = 6.9\) Hz, 2H), 3.25 (bs, 3H), 2.79 (bs, 3H), 1.39 (t, \(J = 6.9\) Hz, 3H). \(^13\)C NMR \(\delta\)(75 MHz, CDCl\(_3\)): 160.4, 152.7, 135.3, 129.1, 127.4, 126.5, 121.8, 112.2, 110.9, 61.2, 37.7, 36.8, 14.1. MS (ESI): m/z = 295 (M+H\(^+\)). HRMS ESI (M+H\(^+\)) \(m/z\) calcd for C\(_{14}\)H\(_{16}\)ClN\(_2\)O\(_3\) (M+H\(^+\)) = 295.08440, found = 295.08401.

Methyl 1-(dimethylcarbamoyl)-1\(H\)-pyrrole-2-carboxylate : (scheme 3, entry 6, 5f)

Isolated yield = 40\%; IR cm\(^{-1}\): 2925, 1704, 1442, 1393, 1292, 1236, 1141, 1093, 1060, 755. \(^1\)H NMR \(\delta\)(300 MHz, CDCl\(_3\)) 6.95 – 6.98 (m, 2H), 6.26 – 6.29 (m, 1H), 3.83 (s, 3H), 3.17 (bs, 3H), 2.71 (bs, 3H). \(^13\)C NMR \(\delta\)(75 MHz, CDCl\(_3\)): 160.4, 153.4, 125, 122.5, 117.5, 110.2, 51.5, 37.7, 36.6. MS (ESI): m/z = 197 (M+H\(^+\)). HRMS ESI (M+H\(^+\)) \(m/z\) calcd for C\(_9\)H\(_{13}\)N\(_2\)O\(_3\) (M+H\(^+\)) = 197.09207, found = 197.09167.
5. Copies of $^1$H NMR and $^{13}$C NMR spectra: compound 3a
Compound 3b

Electronic Supplementary Material (ESI) for Chemical Communications
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Compound 3c
Compound 3d
Compound 3e
Compound 3f
Compound 3h
Compound 3i
Compound 3j
Compound 3k
Compound 3l
Compound 3m
Compound 3n

[Chemical structure image]
Compound 3o
Compound 3q
Compound 3r
Compound 3s
Compound 3t
Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013
Compound 3u
Compound 3v
Compound 5a
Compound 5b

Electronic Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2013
Compound 5c
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Compound 5e
Compound 5f
HPLC data of compound 3r:

A: reaction between L-Phenyl Alanine Methyl Ester and DMF

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B: Reaction between D-Phenyl Alanine Methyl Ester and DMF

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C: Mixture of L + D

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A: (reaction between L-Valine Methyl Ester and DMF)

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