

Expanded Chemistry of Formamidine Ureas

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Supporting Information

General. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-500, AMX-400, or Varian Mercury 200 spectrometers, using CDCl_3 as solvent. Mass spectra were obtained on an Agilent 1100 LC/MS spectrometer (model G1946A) with mobile phase composed of 90:10 $\text{CH}_3\text{OH}:\text{H}_2\text{O}$ containing 0.1% $\text{CF}_3\text{CO}_2\text{H}$. Melting points were measured in a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a MIDAC EM200 instrument with horizontal attenuated total reflectance accessory from Pike Instruments. Column chromatography was performed on EM Science silica gel, 60 Å and 40 μm . TLC analysis was facilitated by the use of the following stains in addition to UV light with fluorescent-indicating plates: phosphomolybdic acid, vanillin/EtOH, anisaldehyde/EtOH, or $\text{KMnO}_4/\text{H}_2\text{O}$. CH_2Cl_2 was dried by passage through activated alumina column;¹ dry Et_3N and the others solvents used in this work were purchased from Aldrich. Reactions requiring anhydrous conditions were performed under nitrogen. Anhydrous magnesium sulfate was used for drying solutions.

General procedure for thiolcarbamate formation.

To a solution of 1-(*tert*-butylimino-methyl)-1,3-dimethyl-urea hydrochloride (**1b**) (2.4 mmol, 1.0 equiv) in dry THF (25 mL) at room temperature under a nitrogen atmosphere was added Et_3N (2.7 mmol, 1.15 equiv). The reaction mixture was stirred for 5 min, after which the corresponding thiol (3.6 mmol, 1.5 equiv) was added. The reaction mixture was refluxed for 12 h, cooled, filtered to remove solid material, and evaporated under vacuum. The residue was purified by column chromatography to yield the thiolcarbamate derivative.

Solvents other than THF and acetonitrile may be used, such as toluene, Et_2O , acetone, or DMF, although lower yields were obtained, and the reaction does proceed well neat (without solvent). At room temperature, it is very sluggish in any solvent. It should be noted that the reactions of **1b** with 4-nitrobenzenethiol and pentachlorothiophenol gave inseparable mixtures of products.

General procedure for N-alkylation/N-acylation of formamidine ureas and reactions with isocyanates.

To a solution of the formamidine urea (1.0 mmol) in dry THF (0.1M) cooled at -78°C under a nitrogen atmosphere was added *n*-BuLi (1.6M solution in hexanes, 0.98 mmol) dropwise. The reaction mixture was stirred for 5 min at -78°C and then 15 min at 0°C . After this time the mixture was cooled again at -78°C and the electrophile (2.0 mmol) was added dropwise. The reaction mixture was allowed to warm to room temperature over ca. 1.5 h and stirred for a further 20 h. The reaction mixture was quickly partitioned between Et_2O and

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saturated aqueous NH_4Cl , washed quickly with brine, dried (MgSO_4), filtered, concentrated, and purified by column chromatography to yield the corresponding formamidine derivative.

With isocyanates R^2NCO , the derived urea ($\text{R}^2\text{NHCONHR}^2$) was always found as a significant byproduct, in addition to many other species observed on TLC. No reaction was observed in the absence of base, even at reflux. The expected acylated structure **13** was never observed. The yields of products **10** were increased by approximately 10% when three equivalents of isocyanate was used. Because of the complex nature of the reaction mixtures, we cannot rule out the formation of both isomers of **10** (**10** and *iso*-**10**, Scheme 5). Indeed, the structure of the major isomer is given based on the similarity of the N-Me chemical shift to other well-characterized formamidine ureas, but should not be regarded as firmly established.

Crossover Experiment (Figure 1). A solution of compound **1b** (6.2 mg, 0.043 mmol) and **1d** (10.0 mg, 0.043 mmol) in 1 mL THF were treated at room temperature with 0.064 mmol (0.74 equiv.) *n*-BuLi. After 30 minutes, the reaction mixture was analyzed by TLC. The two most intense spots corresponded to the starting materials; two other clear spots showed identical R_f 's to **1a** and **1e**, which was verified by co-spotting with authentic materials. Mass spectrometry analysis (direct injection to an Agilent 1100 MSD instrument, with acetonitrile/0.2% TFA mobile phase) is shown in Figure S1.

Infrared Spectroscopy Analysis of Formamidine-Urea + Base (Figure 1). To further establish the proposed base-mediated fragmentation of formamidine ureas, the reaction of compound with *n*-BuLi was followed by IR, as shown in Figure S2. A well-defined band was observed in the characteristic isocyanate region (2227 cm^{-1}).

Compound characterization. Commercially available **2a** and **2e** were found to be identical to the material produced by the reaction of **1b** with the appropriate thiophenol. Compounds **2b**,² **2d**,³ **2i**,⁴ and **4**⁵ have been previously described.

Methylthiocarbamic acid *S*-(4-methoxyphenyl) ester (**2c**). White solid: Mp $90\text{--}91\text{ }^\circ\text{C}$; ^1H NMR (CDCl_3) δ 2.86 (s, 3H), 3.87 (s, 3H), 5.57 (br s, 1H), 6.99 (d, $J = 7.3\text{ Hz}$, 2H), 7.53 (d, $J = 7.6\text{ Hz}$, 2H); ^{13}C NMR (CDCl_3) δ 28.4, 55.8, 115.6, 119.6, 137.7, 161.4, 168.2; IR (thin film, cm^{-1}) 2838, 2053, 1888, 1305, 999, 818; MS m/z (relative intensity) 199 ($\text{M}+2$)⁺ (11), 198 ($\text{M}+1$)⁺ (100). HRMS calcd for $\text{C}_9\text{H}_{12}\text{NO}_2\text{S}$ 198.0583, found 198.0582.

S-(4-hydroxyphenyl) methylthiolcarbamate (**2f**). White semisolid: ^1H NMR (CDCl_3) δ 2.90 (d, $J = 4.3\text{ Hz}$, 3H), 5.49 (br s, 1H), 6.76 (d, $J = 5.1\text{ Hz}$, 2H), 7.34 (d, $J = 5.1\text{ Hz}$, 2H), 8.45 (br s, 1H); ^{13}C NMR (CDCl_3) δ 28.6, 117.4, 118.0, 137.9, 158.6, 168.1; IR (thin film, cm^{-1}) 3024, 2870, 1660, 1591, 1487, 1221, 1004, 827; MS m/z (relative intensity) 206 ($[\text{M}+\text{Na}]^+$) (32), 185 ($\text{M}+2$)⁺ (10), 184 ($\text{M}+1$)⁺ (100). HRMS calcd for $\text{C}_8\text{H}_{10}\text{NO}_2\text{S}$ 184.0427, found 184.0427.

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3) Rinehart, J. K. (PPG Industries, Inc.), **1976**, US Patent # 4055657.

4) Wachter, M. P. (Ortho Pharmaceutical Corp., USA), **1978**, US Patent # 4066681.

5) (a) Almqvist, F.; Guillaume, D.; Hultgren, S. J.; Marshall, G. R. *Tetrahedron Lett.* **1998**, 39, 2293–2294.

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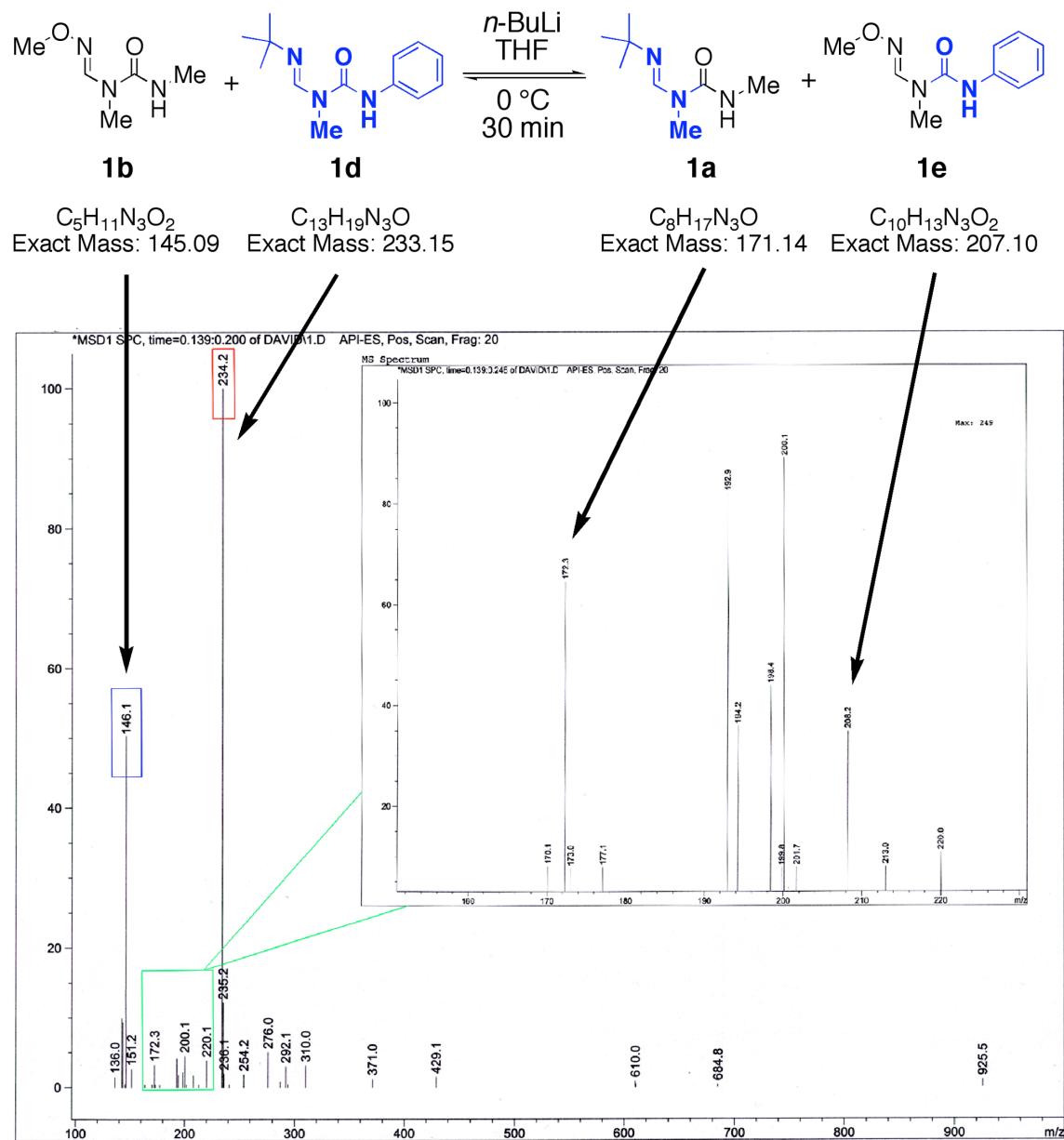
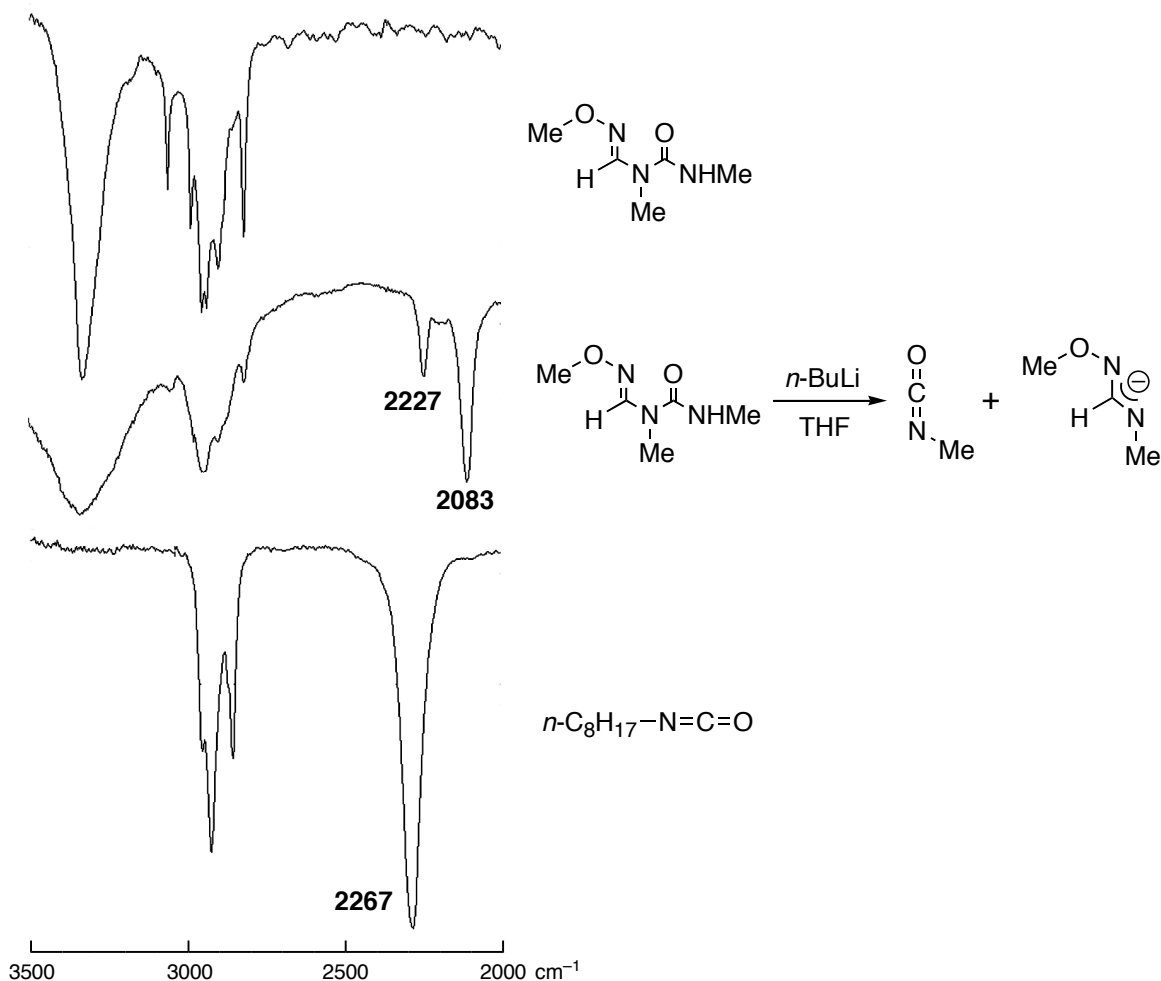
Figure S1. Mass spectrometry of formamidine urea crossover. The inset shows an independent spectrum, focusing on a narrow mass range encompassing **1a** and **1e**.

Figure S2. IR spectroscopic analysis of the treatment of compound **1a** with *n*-BuLi, suggesting the production of methyl isocyanate. The bottom spectrum is that of an analogous alkyl isocyanate, showing the strong NCO stretching band. THF + *n*-BuLi alone show no bands in this region.



S-(2-naphthyl) methylthiolcarbamate (**2g**). White solid: Mp 94–95 °C; ¹H NMR (CDCl₃) δ 2.89 (d, *J* = 4.3 Hz, 3H), 5.53 (br s, 1H), 7.29–7.41 (m, 1H), 7.62–7.68 (m, 3H), 7.91–7.96 (m, 3H); ¹³C NMR (CDCl₃) δ 28.5, 126.2, 127.3, 127.9, 128.2, 128.4, 129.7, 132.2, 133.8, 134.0, 136.0, 167.3; IR (thin film, cm⁻¹) 3278, 3053, 2940, 1680, 1499, 1338, 1226, 1008, 815; MS *m/z* (relative intensity) 240 ([+Na]⁺ (11), 219 (M+2)⁺ (15), 218 (M+1)⁺ (100). HRMS calcd for C₁₂H₁₂NOS 218.0634, found 218.0631.

S-(2-phenylethyl) methylthiolcarbamate (**2h**). Light yellow oil: ¹H NMR (CDCl₃) δ 2.89 (d, *J* = 4.4 Hz, 3H), 2.94 (t, *J* = 8.4 Hz, 2H), 3.18 (t, *J* = 7.4 Hz, 2H), 5.29 (br s, 1H), 7.23–7.31 (m, 5H); ¹³C NMR (CDCl₃) δ 28.4, 31.7, 37.4, 126.9, 128.9, 129.1, 140.7, 168.4; IR (thin film, cm⁻¹)

3212, 3084, 2934, 1670, 1630, 1485, 1223, 1018, 821; MS m/z (relative intensity) 218 ($[\text{M} + \text{Na}]^+$ (4), 197 ($\text{M}+2)^+$ (11), 196 ($\text{M}+1)^+$ (100). HRMS calcd for $\text{C}_{10}\text{H}_{14}\text{NOS}$ 196.0791, found 196.0794.

S-(3-chloropropyl) methylthiolcarbamate (**2k**). Colorless oil: ^1H NMR (CDCl_3) δ 2.07 (q, $J = 6.6$ Hz, 2H), 2.87 (d, $J = 4.8$ Hz, 3H), 3.05 (t, $J = 6.8$ Hz, 2H), 3.62 (t, $J = 4.2$ Hz, 2H), 5.36 (br s, 1H); ^{13}C NMR (CDCl_3) δ 27.3, 28.3, 33.5, 43.8, 167.9; IR (thin film, cm^{-1}) 3308, 2946, 1698, 1634, 1497, 1231, 1010, 813; MS m/z (relative intensity) 190 ($[\text{M} + \text{Na}]^+$ (7), 169 ($\text{M}+2)^+$ (35), 168 ($\text{M}+1)^+$ (100).

S-hexyl methylthiolcarbamate (**2j**). Colorless oil: ^1H NMR (CDCl_3) δ 0.88 (t, $J = 7.7$ Hz, 3H), 1.27–1.43 (m, 6H), 1.54–1.65 (m, 2H), 2.87 (d, $J = 4.2$ Hz, 3H), 2.88–2.94 (m, 2H), 5.30 (br s, 1H); ^{13}C NMR (CDCl_3) δ 14.4, 22.9, 28.8, 28.3, 30.4, 30.9, 31.7, 168.5; IR (thin film, cm^{-1}) 3312, 2938, 2861, 1662, 1509, 1219, 1018, 821; MS m/z (relative intensity) 198 ($[\text{M} + \text{Na}]^+$ (8), 177 ($\text{M}+2)^+$ (11), 176 ($\text{M}+1)^+$ (100).

Ethyl 3-{[(methylamino)carbonyl]sulfanyl}propanoate (**2l**). Light yellow oil: ^1H NMR (CDCl_3) δ 1.26 (t, $J = 11.2$ Hz, 3H), 2.68 (t, $J = 11.2$ Hz, 2H), 2.87 (d, $J = 5.2$ Hz, 3H), 3.15 (t, $J = 7.4$ Hz, 2H), 4.15 (c, $J = 7.2$ Hz, 2H), 5.31 (br s, 1H); ^{13}C NMR (CDCl_3) δ 14.4, 25.2, 28.1, 35.8, 61.0, 167.7, 172.3; IR (thin film, cm^{-1}) 3224, 2950, 1734, 1658, 1517, 1215, 1014, 809; MS m/z (relative intensity) 214 ($[\text{M} + \text{Na}]^+$ (66), 193 ($\text{M}+2)^+$ (9), 192 ($\text{M}+1)^+$ (100). HRMS calcd for $\text{C}_7\text{H}_{14}\text{NO}_3\text{S}$ 192.0689, found 192.0687.

S-(4-hydroxybutyl) methylthiolcarbamate (**2m**). Light yellow oil: ^1H NMR (CDCl_3) δ 1.63–1.73 (m, 4H), 2.87 (d, $J = 4.7$ Hz, 3H), 2.95 (t, $J = 6.3$ Hz, 2H), 3.68 (t, $J = 6.3$ Hz, 2H), 5.34 (br s, 1H); ^{13}C NMR (CDCl_3) δ 27.2, 28.1, 29.8, 31.8, 62.0, 168.9; IR (thin film, cm^{-1}) 3296, 2918, 1082, 1634, 1497, 1312, 1235, 1002, 809; MS m/z (relative intensity) 173 ($\text{M}+2)^+$ (11), 172 ($\text{M}+1)^+$ (100).

S-[2-(butylamino)ethyl] methylthiolcarbamate (**2n**). Light yellow oil: ^1H NMR (CDCl_3) δ 0.94 (t, $J = 7.4$ Hz, 3H), 1.30–1.43 (m, 2H), 1.44–1.57 (m, 2H), 2.63–2.74 (m, 2H), 2.80 (d, $J = 4.6$ Hz, 3H), 3.18 (t, $J = 6.8$ Hz, 2H), 3.41 (t, $J = 7.0$ Hz, 2H), 4.36 (br s, 1H), 4.44 (br s, 1H); ^{13}C NMR (CDCl_3) δ 14.3, 20.5, 27.9, 29.9, 31.1, 48.1, 51.4, 158.9; IR (thin film, cm^{-1}) 3348, 2958, 2873, 1666, 1618, 1489, 1296, 1240, 946; MS m/z (relative intensity) 192 ($\text{M}+2)^+$ (10), 191 ($\text{M}+1)^+$ (100). HRMS calcd for $\text{C}_8\text{H}_{19}\text{N}_2\text{OS}$ 191.1213, found 191.1212.

S-(8-sulfanyloctyl) methylthiolcarbamate (**2o**). White solid: Mp 43–44 °C; ^1H NMR (CDCl_3) δ 1.30–1.35 (m, 8H), 1.60 (m, 4H), 2.52 (m, 2H), 2.88 (d, $J = 4.8$ Hz, 3H), 2.89–2.95 (m, 2H), 5.29 (br s, 1H); ^{13}C NMR (CDCl_3) δ 25.0, 28.2, 28.6, 29.0, 29.3, 29.4, 30.3, 30.9, 34.3, 168.5; IR (thin film, cm^{-1}) 3336, 2930, 2853, 1646, 1529, 1465, 1227, 821; MS m/z (relative intensity) 258 ($[\text{M} + \text{Na}]^+$ (8), 237 ($\text{M}+2)^+$ (13), 236 ($\text{M}+1)^+$ (100). HRMS calcd for $\text{C}_{10}\text{H}_{22}\text{NOS}_2$ 236.1137, found 236.1134.

Thiazoline **4** was reduced to the corresponding hydroxymethyl compound by NaBH₄ as previously described.^{5b} The compound we obtained showed $[\alpha]_D^{25} = +89^\circ$, identical within experimental error to the reported value of $+93^\circ$.^{5b}

(4*R*,5*R*)-4,5-Diphenyl-4,5-dihydro-1*H*-imidazole (**8**). To a solution of 1-(*tert*-butylimino-methyl)-1,3-dimethyl-urea hydrochloride (207 mg, 1.0 mmol) in dry CH₂Cl₂ (2 mL, 0.5M in formamidine) at room temperature under a nitrogen atmosphere was added Et₃N (156 μ L, 1.1 mmol). The reaction mixture was stirred for 5 min, after which time was heated at 50 °C and (1*R*,2*R*)-(+)-1,2-diphenylethylenediamine (318 mg, 1.5 mmol) was added. The reaction mixture was refluxed for 3h, after which time the solvent was evaporated. The residue was triturated with THF, filtered, concentrated and recrystallized from ethyl acetate to afford **8** in 62% yield. Colorless solid: Mp 99–101 °C; $[\alpha]_D^{20} +341^\circ$ ($c=0.63$, CH₃OH) ¹H NMR (CDCl₃) δ 4.71 (s, 2H), 7.26 (d, $J = 7.0$ Hz, 4H), 7.30 (d, $J = 6.6$ Hz, 2H), 7.35 (d, $J = 7.0$ Hz, 4H); ¹³C NMR (CDCl₃) δ 126.9, 127.9, 129.1, 143.6, 153.9; IR (thin film, cm⁻¹) 3346, 2920, 1631, 1581, 1410, 1276, 1179; MS m/z (relative intensity) 224 (M+2)⁺ (18), 223 (M+1)⁺ (100). HRMS calcd for C₁₅H₁₅N₂ 223.1230, found 223.1230. The *meso* form of this compound has been described.⁶

1-(*tert*-Butylimino-methyl)-1,3,3-trimethyl urea (**9a**). Colorless oil: ¹H NMR (CDCl₃) δ 1.20 (s, 9H), 2.90 (s, 3H), 3.00 (s, 3H), 3.09 (s, 3H), 7.96 (br s, 1H); ¹³C NMR (CDCl₃) δ 31.1, 32.6, 38.7, 38.9, 54.9, 147.5, 163.4; IR (thin film, cm⁻¹) 3480, 2926, 1665, 1487, 1373, 1306, 1115; MS m/z (relative intensity) 187 (M+2)⁺ (10), 186 (M+1)⁺ (100). HRMS calcd for C₉H₂₀N₃O 186.1601, found 186.1601.

1-(*tert*-Butylimino-methyl)-1,3-dimethyl-3-octyl urea (**9b**). Colorless oil: ¹H NMR (CDCl₃) δ 0.91 (t, $J = 6.9$ Hz, 3H), 1.24 (s, 3H), 1.24–1.33 (m, 12H), 2.92 (s, 3H), 3.12 (s, 3H), 3.27 (t, $J = 6.6$ Hz, 2H), 7.98 (br s, 1H); ¹³C NMR (CDCl₃) δ 14.5, 23.0, 27.1, 27.7, 29.6, 31.1, 32.1, 32.7, 36.6, 50.9, 54.9, 147.6, 162.2; IR (thin film, cm⁻¹) 3438, 2935, 2862, 1657, 1480, 1382, 1305, 1211, 1087; MS m/z (relative intensity) 285 (M+2)⁺ (18), 284 (M+1)⁺ (100). HRMS calcd for C₁₆H₃₄N₃O 284.2696, found 284.2694.

1-(*tert*-Butylimino-methyl)-1,3-dimethyl-3-prop-2-ynyl-urea (**9c**). Colorless oil: ¹H NMR (CDCl₃) δ 1.20 (s, 9H), 2.30 (br s, 1H), 2.96 (s, 3H), 3.11 (s, 3H), 3.98 (s, 2H), 8.01 (br s, 1H); ¹³C NMR (CDCl₃) δ 31.1, 32.6, 36.5, 40.5, 55.1, 73.1, 79.1, 147.1, 161.7; IR (thin film, cm⁻¹) 3266, 2967, 1659, 1478, 1374, 1303, 1209, 1109; MS m/z (relative intensity) 211 (M+2)⁺ (14), 210 (M+1)⁺ (100). HRMS calcd for C₁₀H₂₀N₃O 210.1601, found 210.1604. Anal. Calcd for C₁₀H₁₉N₃O: C, 63.13; H, 9.15, N, 20.08. Found: C, 63.10; H, 9.19, N, 20.12.

1-Benzoyl-3-(*tert*-butylimino-methyl)-1,3-dimethyl-urea (**9d**). White solid: Mp 58–59 °C; ¹H NMR (CDCl₃) δ 1.21 (s, 9H), 2.93 (s, 3H), 3.33 (s, 3H), 7.36–7.39 (m, 2H), 7.46–7.51 (m, 3H), 7.98 (br s, 1H); ¹³C NMR (CDCl₃) δ 30.5, 34.4, 55.7, 128.1, 128.9, 132.3, 135.2, 143.8, 162.2, 171.5; IR (thin film, cm⁻¹) 2969, 1654, 1436, 1316, 1212, 1084; MS m/z (relative intensity) 187 (M+2)⁺ (10), 186 (M+1)⁺ (100). HRMS calcd for C₁₅H₂₂N₃O₂ 276.1706, found 276.1712.

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1-(Benzylimino-methyl)-1,3,3-trimethyl-urea (**9e**). Colorless oil: ^1H NMR (CDCl_3) δ 2.90 (s, 3H), 2.99 (s, 3H), 3.07 (s, 3H), 4.57 (s, 2H), 7.26–7.33 (m, 5H), 8.63 (br s, 1H); ^{13}C NMR (CDCl_3) δ 30.0, 38.6, 38.8, 60.2, 127.7, 128.7, 140.8, 152.3, 163.4; IR (thin film, cm^{-1}) 3431, 2935, 1660, 1546, 1489, 1382, 1318, 1120, 1073; MS m/z (relative intensity) 221 ($\text{M}+2$) $^+$ (15), 220 ($\text{M}+1$) $^+$ (100). HRMS calcd for $\text{C}_{12}\text{H}_{18}\text{N}_3\text{O}$ 220.1444, found 220.1445.

1-[(E)-[(Benzyloxy)imino]methyl]-1,3,3-trimethyl-urea (**9f**). Colorless oil: ^1H NMR (CDCl_3) δ 2.86 (s, 6H), 3.04 (s, 3H), 4.96 (s, 2H), 7.29–7.36 (m, 5H), 8.26 (br s, 1H); ^{13}C NMR (CDCl_3) δ 33.4, 39.0, 76.4, 128.3, 128.8, 128.9, 138.0, 148.9, 160.8; IR (thin film, cm^{-1}) 3503, 2936, 1672, 1625, 1494, 1444, 1370, 1262, 1128, 1055; MS m/z (relative intensity) 237 ($\text{M}+2$) $^+$ (14), 236 ($\text{M}+1$) $^+$ (100). HRMS calcd for $\text{C}_{12}\text{H}_{18}\text{N}_3\text{O}_2$ 236.1393, found 236.1392.

1-Hexanoyl-3-[(E)-[(benzyloxy)imino]methyl]-1,3-dimethyl-urea (**9g**). Colorless oil: ^1H NMR (CDCl_3) δ 0.89 (t, $J = 7.0$ Hz, 3H), 2.28 (m, 6H), 2.35 (m, 2H), 3.20 (s, 3H), 3.09 (s, 3H), 5.01 (s, 2H), 7.26–7.39 (m, 5H), 8.36 (br s, 1H); ^{13}C NMR (CDCl_3) δ 14.3, 22.8, 25.0, 31.7, 32.2, 33.8, 35.4, 77.1, 128.5, 128.9, 129.0, 137.4, 145.6, 157.3, 174.4; IR (thin film, cm^{-1}) 2955, 2932, 2861, 1697, 1620, 1459, 1352, 1292, 1097, 1037; MS m/z (relative intensity) 342 ($\text{M}+\text{Na}$) $^+$ (100), 321 ($\text{M}+2$) $^+$ (4), 320 ($\text{M}+1$) $^+$ (15). HRMS calcd for $\text{C}_{17}\text{H}_{26}\text{N}_3\text{O}_3$ 320.1969, found 320.1970.

1-[(E)-(Methoxyimino)methyl]-1,3,3-trimethyl-urea (**9h**). Colorless oil: ^1H NMR (CDCl_3) δ 2.88 (s, 6H), 3.05 (s, 3H), 3.74 (s, 3H), 8.20 (br s, 1H); ^{13}C NMR (CDCl_3) δ 32.3, 37.6, 60.7, 147.2, 159.3; IR (thin film, cm^{-1}) 3514, 2944, 1663, 1626, 1502, 1384, 1270, 1129, 1056; MS m/z (relative intensity) 261 ($\text{M}+2$) $^+$ (8), 260 ($\text{M}+1$) $^+$ (100). HRMS calcd for $\text{C}_6\text{H}_{14}\text{N}_3\text{O}_2$ 160.1080, found 160.1083. Anal. Calcd for $\text{C}_6\text{H}_{13}\text{N}_3\text{O}_2$: C, 45.27; H, 8.23, N, 26.40. Found: C, 45.29; H, 8.30, N, 26.48.

1-Benzoyl-3-[(E)-(methoxyimino)methyl]-1,3-dimethyl-urea (**9i**). Colorless oil: ^1H NMR (CDCl_3) δ 2.93 (s, 3H), 3.29 (s, 3H), 3.69 (s, 3H), 7.36–7.39 (m, 2H), 7.46–7.51 (m, 3H), 8.22 (br s, 1H); ^{13}C NMR (CDCl_3) δ 32.2, 34.6, 62.5, 127.9, 129.0, 132.4, 135.1, 144.8, 157.4, 171.4; IR (thin film, cm^{-1}) 2949, 1688, 1433, 1359, 1178, 1068; MS m/z (relative intensity) 273 ($\text{M}+2$) $^+$ (16), 272 ($\text{M}+1$) $^+$ (100). HRMS calcd for $\text{C}_{12}\text{H}_{16}\text{N}_3\text{O}_3$ 250.1186, found 250.1189. Anal. Calcd for $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_3$: C, 57.82; H, 6.07, N, 16.86. Found: C, 57.83; H, 6.09, N, 16.85.

1-(*tert*-Butylimino)-3-hexyl-1-methyl-urea (**10a**). White solid: Mp 63–64 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 0.94 (t, $J = 6.3$ Hz, 3H), 1.26 (s, 9H), 1.27–1.39 (m, 7H), 1.57–1.60 (m, 1H), 3.20 (s, 2H), 3.36 (t, $J = 6.3$ Hz, 2H), 7.2 (s, 0.5H), 7.70 (s, 0.5H); ^{13}C NMR (CDCl_3) δ 14.4, 23.0, 27.2, 29.9, 30.8, 31.9, 40.3, 55.1, 178.8, 156.6; IR (thin film, cm^{-1}) 3347, 2958, 2928, 2864, 1666, 1546, 1462, 1321, 1210, 1076; MS m/z (relative intensity) 243 ($\text{M}+2$) $^+$ (17), 242 ($\text{M}+1$) $^+$ (100). HRMS calcd for $\text{C}_{13}\text{H}_{27}\text{N}_3\text{O}$ 242.2227, found 242.2229.

1-(*tert*-Butylimino-methyl)-3-phenyl-1-methyl-urea (**10b**). Colorless oil: ^1H NMR (CDCl_3) δ 1.29 (s, 9H), 3.23 (s, 3H), 7.04–7.06 (m, 1H), 7.28–7.32 (m, 2H), 7.52–7.54 (m, 2H), 7.66 (s, 1H); ^{13}C NMR (CDCl_3) δ 30.8, 35.3, 55.5, 120.1, 123.5, 129.3, 139.5, 149.1, 153.9; IR (thin film, cm^{-1}) 3316, 2964, 1669, 1596, 1549, 1448, 1317, 1237, 1076; MS m/z (relative intensity)

256 (M+Na)⁺ (100), 235 (M+2)⁺ (6), 234 (M+1)⁺ (14). HRMS calcd for C₁₃H₂₀N₃O 234.1601, found 234.1603.

1-[(*E*)-(Methoxyimino)methyl]-3-phenyl-1-methyl-urea (**10c**). Gummy syrup: ¹H NMR (CDCl₃) δ 3.21 (s, 3H), 3.85 (s, 3H), 7.10 (m, 1H), 7.30–7.34 (m, 2H), 7.47–7.48 (m, 2H), 8.14 (s, 1H), 9.61 (br s, 1H); ¹³C NMR (CDCl₃) δ 34.9, 62.6, 120.7, 124.4, 129.4, 138.5, 148.2, 152.7; IR (thin film, cm⁻¹) 3319, 3058, 2947, 2236, 1672, 1609, 1531, 1451, 1360, 1307, 1243, 1162, 1065; MS *m/z* (relative intensity) 230 (M+Na)⁺ (100), 209 (M+2)⁺ (4), 208 (M+1)⁺ (11). HRMS calcd for C₁₀H₁₄N₃O₂ 208.1080, found 208.1081. Anal. Calcd for C₁₀H₁₃N₃O₂: C, 57.96; H, 6.32, N, 20.28. Found: C, 57.99; H, 6.32, N, 20.31.

1-[(*E*)-(Methoxyimino)methyl]-3-(4-bromo-phenyl)-1-methyl-urea (**10d**). White solid: Mp 75–76 °C; ¹H NMR (CDCl₃) δ 3.21 (s, 3H), 3.27 (s, 2.3H), 3.84 (s, 3.3H), 7.30–7.47 (m, 7H), 8.06 (s, 1H), 9.89 (br s, 1H); ¹³C NMR (CDCl₃) δ 34.3, 35.0, 62.6, 120.4, 120.6, 120.7, 123.6, 124.4, 125.6, 129.4, 136.8, 138.5, 148.2, 150.2, 152.7; IR (thin film, cm⁻¹) 3319, 2937, 2246, 1706, 1612, 1535, 1491, 1307, 1253, 1065; MS *m/z* (relative intensity) 309 (M+Na)⁺ (100), 287 (M+2)⁺ (5), 286 (M+1)⁺ (13). HRMS calcd for C₁₀H₁₃BrN₃O₂ 286.0186, found 286.0191.

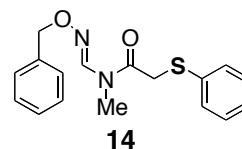
2-Bromo-*N*-methyl-*N'*-[(*E*)-(benzyloxyimino)methyl]-acetamide (**11**). A solution of the 1-[(*E*)-(benzyloxyimino)methyl]-1,3-dimethylurea (221 mg, 1.0 mmol) and 2,6-lutidine (71 μ L, 0.98 mmol) in dry CH₂Cl₂ (5 mL, 0.2M) was cooled at –78 °C under a nitrogen atmosphere and stirred for 15 min before the addition of bromoacetyl bromide (freshly distilled) (81 μ L, 0.94 mmol). The reaction mixture was slowly warmed to room temperature over ca. 2 h and stirred for a further 24 h. The mixture was concentrated under vacuum and partitioned with CH₂Cl₂ and aqueous saturated solution of NH₄Cl, washed with brine, dried (MgSO₄), filtered, concentrated and purified by column chromatography to afford the corresponding formamidine derivatives in 68% yield (193 mg [**11** + **12**], ratio 10:1). Colorless oil: ¹H NMR (CDCl₃) δ 3.20 (s, 3H), 3.30 (s, 3H), 3.93 (s, 4H), 5.05 (s, 4H), 7.26–7.38 (m, 10H), 8.47 (br s, 1H), 8.83 (br s, 1H); ¹³C NMR (CDCl₃) δ 25.5, 26.2, 30.1, 32.5, 128.4, 128.6, 128.9, 137.3, 144.5, 145.3, 165.7, 166.6; IR (thin film, cm⁻¹) 3034, 2940, 1685, 1621, 1444, 1356, 1293, 1088, 1044; MS *m/z* (relative intensity) 309(307) (M+Na)⁺ (100), 287(285) (M+1)⁺ (93). HRMS calcd for C₁₁H₁₄BrN₂O₂ 285.0233, found 285.0231.

1-(2-Bromo-acetyl)-1,3-dimethyl-3-[(*E*)-[(benzyloxyimino)methyl]]-urea (**12**). [1-[(*E*)-(benzyloxyimino)methyl]-1,3-dimethylurea + bromoacetyl bromide] Colorless oil: ¹H NMR (CDCl₃) δ 3.10 (s, 3H), 3.20 (s, 3H), 4.08 (s, 2H), 5.03 (s, 2H), 7.33–7.40 (m, 5H), 8.35 (br s, 1H); ¹³C NMR (CDCl₃) δ 27.4, 32.6, 34.5, 77.1, 128.6, 128.8, 128.9, 137.3, 145.3, 156.7, 168.9; IR (thin film, cm⁻¹) 2919, 1694, 1624, 1436, 1345, 1288, 1094, 1037; MS *m/z* (relative intensity) 366(364) (M+Na)⁺ (28), 344(342) (M+1)⁺ (100). HRMS calcd for C₁₃H₁₆BrN₃O₃ 342.0448, found 342.0445.

The identity of compound **11** was further established by reaction with thiophenol to give *N*-Methyl-*N'*-[(*E*)-(benzyloxyimino)methyl]-2-phenylsulfanyl-acetamide (**14**), as follows. To a solution of 2-bromo-*N*-methyl-*N'*-[(*E*)-(benzyloxyimino)methyl]-acetamide (**11**) (284 mg, 1.0 mmol) and Et₃N (142 μ L, 1.0 mmol) in dry CH₂Cl₂ (5 mL, 0.2M) was added thiophenol (106 μ L, 1.0 mmol) at 0 °C under a nitrogen atmosphere. This mixture was allowed to stir for 20 min.

The solution was then washed with water, dried (MgSO_4), filtered, concentrated and purified by column chromatography to give the formamidine derivative **14** in 92% yield (288.8 mg). Colorless oil: ^1H NMR (CDCl_3) δ 3.13 (s, 3H), 3.23 (s, 3H), 3.80 (s, 4H), 5.02 (s, 4H), 7.26–7.38 (m, 15H), 8.49 (br s, 1H), 8.84 (br s, 1H); ^{13}C NMR (CDCl_3) δ 29.8, 32.3, 37.7, 37.9, 128.1, 128.2, 128.3, 128.6, 128.8, 128.9, 129.1, 129.6, 131.5, 131.6, 144.8, 145.6, 167.6, 168.8; IR (thin film, cm^{-1}) 3059, 2924, 1683, 1619, 1445, 1364, 1300, 1099; MS m/z (relative intensity) 337 ($\text{M}+\text{Na}$) $^+$ (63), 316 ($\text{M}+2$) $^+$ (20), 315 ($\text{M}+1$) $^+$ (100). HRMS calcd for $\text{C}_{17}\text{H}_{19}\text{N}_2\text{O}_2\text{S}$ 315.1162, found 315.1163.

Compounds **11** and **14** display two rotameric forms in their ^1H and ^{13}C NMR spectra, identified by coalescence upon heating, as shown below for **14**.



NMR Spectra begin on the next page.

