Supporting Information

An Efficient Procedure for the Preparation of 4-Substituted-5-aminoimidazoles

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Contents: Experimental procedures and analytical data for the following compounds are presented – **9, 10, 11, 12, 13a, 13b, 14a, 14b, 15a, 15b, 17, 21, 22, 23, 24, 26, 27a-h, 28a-g, 29a-l, 30, 31a-f, 32a-j.**

Experimental Section

General Methods. Diethyl ether and tetrahydrofuran were distilled from sodium/benzophenone immediately before use. Dichloromethane, acetonitrile, *N,N*-dimethylformamide, pyridine, triethylamine and benzylamine were distilled from calcium hydride before use. Methanol was distilled from magnesium turnings. All reactions were performed under an atmosphere of nitrogen in standard glassware unless otherwise noted. Following aqueous work-ups organic solutions were dried over anhydrous magnesium sulfate before the solvent was removed under reduced pressure on a rotary evaporator. Thin layer chromatography was conducted using aluminum-backed silica plates and column chromatography was performed using silica gel (230-400 mesh). Melting points were obtained on an

open capillary apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ (unless otherwise noted) at 300 MHz for ^1H NMR and 100 MHz for ^{13}C NMR. Chemical shifts are reported relative to the standard ppm value for the solvent used. DEPT experiments were used to assign ^{13}C NMR spectra. Elemental analyses were performed by the Analytical Laboratory, College of Chemistry, University of California, Berkeley, CA.

Compounds **8a**,[1] **8b**,[2] **19**,[3, 4] **20**,[5] and **26**[6] were prepared according to literature procedures and provided analytical data that were in agreement with those already published.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-methanesulfonyloxypropionamide (9). A mixture of alcohol **8a** (167 mg, 0.82 mmol) and triethylamine (0.17 mL, 1.23 mmol, 150 mol%) in CH_2Cl_2 (10 mL) was cooled to 0 °C. To this mixture was added, dropwise, methanesulfonyl chloride (64 μL, 0.82 mmol, 100 mol%) and the mixture was then stirred for 15 min before it was diluted with EtOAc and filtered through a pad of silica. The filtrate was carefully (water bath temperature < 20 °C) concentrated to afford the mesylate as a white solid (208 mg, 90%): mp 111-115 °C; ^1H NMR δ 1.46 (s, 9H), 3.06 (s, 3H), 4.35-4.40 (dd, 1H, J = 10.2, 4.4 Hz), 4.47-4.57 (br, 1H), 4.62-4.66 (dd, 1H, J = 10.2, 4.2 Hz), 5.50-5.56 (br, 1H), 5.86-5.92 (br, 1H), 6.46-6.55 (br, 1H); ^{13}C NMR δ 28.2 (CH_3), 37.4 (CH_3), 68.8 (CH), 73.8 (C), 93.5 (CH_2), 155.4 (C), 171.0 (C). Anal. Calcd for $C_9H_{18}N_2O_6S$: C, 38.29; H, 6.43; N, 9.92. Found: C, 38.46; H, 6.57; N, 9.80.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-azidopropionamide (10). To a solution of mesylate **9** (17 mg, 60 μmol) in DMF (3 mL) was added sodium azide (8 mg, 0.12 mmol, 200 mol%) and the mixture was stirred at room temperature for 24 h. After this time, the solvent was evaporated to leave a white solid residue, which was extracted with CH_2Cl_2 (20 mL). The mixture was then filtered and the filtrate was evaporated to afford the azide as a white solid (13 mg, 95%): mp 68-69 °C; ^1H NMR δ 1.45 (s, 9H), 3.52-3.58 (dd, 1H, J = 12.3, 5.6 Hz), 3.81-3.87 (dd, 1H, J = 12.3, 4.7 Hz), 4.29-4.35 (br, 1H), 5.37-5.41 (d, 1H, J = 7.1 Hz), 5.85-5.94 (br, 1H) and 6.38-6.44 (br, 1H); ^{13}C NMR δ 28.2 (CH_3), 53.2 (CH), 53.6 (CH_2), 80.8 (C), 155.5 (C) and 174.1 (C). Anal. Calcd for $C_8H_{15}N_5O_3$: C, 41.92; H, 6.60; N, 30.55. Found: C, 42.31; H, 6.75; N, 30.19.

General Procedure A. Dehydration of Amides to Nitriles. To a solution of the primary amide (100 mol%) and *para*-toluenesulfonyl chloride (200 mol%) in CH_2Cl_2 (0.4 M) was added pyridine (500 mol%). After complete reaction as judged by TLC sat. aq. $NaHCO_3$ was carefully added. The resultant two-phase mixture was stirred vigorously for 2 h before the layers were separated and the organic phase was washed with 1 M aq. HCl and then another portion of sat. aq. $NaHCO_3$. The aqueous phases were back extracted with CH_2Cl_2 and the combined organic phase was dried, filtered and concentrated to leave a crude product. This crude product was purified by column chromatography using an EtOAc/hexanes gradient as the eluent.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-azidopropanenitrile (11). Prepared according to General Procedure A. Primary amide **10** (500 mg, 2.18 mmol) afforded the nitrile as a white solid (456 mg, 99%): mp 64-65 °C; ^{1}H NMR δ 1.45 (s, 9H), 3.57-3.63 (dd, 1H, J = 12.5, 5.1 Hz), 3.69-3.75 (dd, 1H, J = 12.5, 4.9 Hz), 4.70-4.82 (br, 1H) and 5.37-5.40 (br d, 1H, J = 8.7 Hz). ^{13}C NMR δ 28.2 (CH_3), 42.2 (CH_2), 52.4 (CH), 81.9 (C), 116.8 (C) and 154.1 (C). Anal. Calcd for $C_8H_{13}N_5O_2$: C, 45.49; H, 6.20; N, 33.16. Found: C, 45.86; H, 6.46; N, 32.91.

General Procedure B. Deprotection of *N*-Boc α-Aminonitriles. Trifluoroacetic acid (1000 mol%) was cooled to –15 °C and then the protected α-aminonitrile (100 mol%) was added neat. The mixture was then stirred at –15 °C for 5 h. After this time, the mixture was transferred slowly using a cannula into a mixture of conc. NH_4OH/water cooled to –10 °C. The mixture was then extracted with CH_2Cl_2 and the combined organic phase was dried, filtered and concentrated to leave a crude oil. This oil was purified by column chromatography using an EtOAc/hexanes gradient as the eluent.

(*S*)-2-Amino-3-azidopropanenitrile (12). Prepared according to General Procedure B. Protected compound **11** (10.50 g, 49.7 mmol) afforded the α-aminonitrile as a colorless oil (2.32 g, 42%): ^{1}H NMR δ 1.68-1.80 (br, 2H), 3.53-3.67 (m, 2H), 3.84-3.87 (t, 1H, J = 5.4 Hz); ^{13}C NMR δ 43.4 (CH_2), 54.2 (CH), 120.1 (C). Anal. Calc. For $C_3H_5N_5$: C, 32.43; H, 4.54; N, 63.03. Found: C, 32.63; H, 4.74; N, 62.80.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-[(*tert*-butyldimethylsilyl)oxy]propionamide (13a). To a solution of serine amide **8a** (1.07 g, 5.2 mmol) and imidazole (0.71 g, 10.4 mmol, 200 mol%) in CH_2Cl_2 (30 mL) was added a solution of TBSCl (0.79 g, 5.2 mmol, 100 mol%) in CH_2Cl_2 (20 mL) and then DMAP (6 mg, 52.0 μmol, 1 mol%). The mixture was stirred for 48 h before it was quickly washed with 0.5 M aq. HCl (50 mL). The combined organic phase was then dried, filtered and concentrated to leave a colorless oil, which was purified by column chromatography using 40% EtOAc/hexanes as the eluent. Evaporation of the solvent afforded the silylated serine amide as a white solid (1.57 g, 94%): mp 82-84 °C; ^{1}H NMR δ 0.09 (s, 6H), 0.86 (s, 9H), 1.42 (s, 9H), 3.60-3.65 (t, 1H, *J* = 9.8 Hz), 3.95-4.00 (dd, 1H, *J* = 9.8, 4.0 Hz), 4.05-4.20 (br, 1H), 5.40-5.42 (d, 1H, *J* = 6.6 Hz), 6.12-6.28 (br, 1H), 6.46-6.58 (br, 1H); ^{13}C NMR δ -5.6 (CH_3), -5.5 (CH_3), 18.2 (C), 25.8 (CH_3), 28.3 (CH_3), 55.2 (CH), 63.2 (CH_2), 80.0 (C), 155.5 (C), 173.3 (C). Anal. Calc. For $C_{14}H_{30}N_2O_4Si$: C, 52.80; H, 9.49; N, 8.80. Found: C, 52.82; H, 9.48; N, 8.81.

(*2S*,*3R*)-*2*-[(*tert*-Butoxycarbonyl)amino]-3-[(*tert*-butyldimethylsilyl)oxy]butyramide (13b). To a solution of threonine amide **8b** (3.36 g, 15.4 mmol) and imidazole (2.10 g, 30.8 mmol, 200 mol%) in CH_2Cl_2 (60 mL) was added a solution of TBSCl (2.32 g, 15.4 mmol, 100 mol%) in CH_2Cl_2 (20 mL) then DMAP (2 mg, 15 μmol, 1 mol%). The mixture was stirred for 48 h before it was quickly washed with 0.5 M aq. HCl (70 mL). The combined organic phase was then dried, filtered and concentrated to leave a colorless oil, which was purified by column chromatography using 40% EtOAc/hexanes as the eluent. Evaporation of the solvent afforded the silylated threonine amide as a colorless oil (4.78 g, 96%): ^{1}H NMR δ 0.07 (s, 3H), 0.09 (s, 3H), 0.89 (s, 9H), 1.15-1.17 (d, 3H, *J* = 6.3 Hz), 1.49 (s, 9H), 4.09-4.18 (br, 1H), 4.38-4.41 (m, 1H), 5.42-5.55 (br, 2H), 6.59-6.69 (br, 1H); ^{13}C NMR δ -5.0 (CH_3), -4.7 (CH_3), 17.6 (CH_3), 18.6 (C), 25.8 (CH_3), 28.3 (CH_3), 59.1 (CH), 68.1 (CH), 79.9 (C), 155.7 (C), 172.6 (C). Anal. Calc. For $C_{15}H_{32}N_2O_4Si$: C, 54.18; H, 9.70; N, 8.42. Found: C, 54.21; H, 9.80; N, 8.15.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-3-[(*tert*-butyldimethylsilyl)oxy]propanenitrile (14a). Prepared according to General Procedure A. Primary amide **13a** (1.01 g, 3.17 mmol) afforded the nitrile as a colorless oil (0.91 g, 96%): ^{1}H NMR δ 0.09 (s, 3H), 0.10 (s, 3H), 0.90 (s, 9H), 1.45 (s, 9H), 3.74-

3.79 (dd, 1H, J = 10.3, 4.3 Hz), 3.84-3.88 (dd, 1H, J = 10.3, 3.4 Hz), 4.58-4.66 (br, 1H), 5.18-5.25 (br, 1H); ^{13}C NMR δ -5.2 (CH_3), -5.1 (CH_3), 18.3 (C), 25.7 (CH_3), 28.2 (CH_3), 44.5 (CH), 63.3 (CH_2), 81.2 (C), 117.8 (C), 154.4 (C). Anal. Calc. For $C_{14}H_{28}N_2O_2Si$: C, 55.96; H, 9.39; N, 9.32. Found: C, 55.91; H, 9.14; N, 9.52.

(2*S*,3*R*)-*2*-[(*tert*-Butoxycarbonyl)amino]-3-[(*tert*-butyldimethylsilyl)oxy]butanenitrile (14b). Prepared according to General Procedure A. Primary amide **13b** (1.15 g, 3.6 mmol) afforded the nitrile as a colorless oil (1.02 g, 94%): ^{1}H NMR δ 0.11 (s, 3H), 0.16 (s, 3H), 0.91 (s, 9H), 1.20-1.22 (d, 3H, J = 6.0 Hz), 1.47 (s, 9H), 4.11-4.18 (m, 1H), 4.46-4.53 (br, 1H), 4.97-5.06 (br, 1H); ^{13}C NMR δ -4.9 (CH_3), -4.6 (CH_3), 18.0 (C), 19.9 (CH_3), 25.7 (CH_3), 28.2 (CH_3), 48.7 (CH), 68.5 (CH), 81.2 (C), 118.3 (C), 154.8 (C). Anal. Calc. For $C_{15}H_{30}N_2O_3Si$: C, 57.29; H, 9.61; N, 8.91. Found: C, 56.95; H, 9.70; N, 8.64.

(*S*)-2-Amino-3-[(*tert*-butyldimethylsilyl)oxy]propanenitrile (15a). Prepared according to General Procedure B. Protected compound **14a** (9.75 g, 32.4 mmol) afforded the α-aminonitrile as a colorless oil (2.86 g, 44%): ^{1}H NMR δ 0.10 (s, 3H), 0.12 (s, 3H), 0.92 (s, 9H), 1.71-1.84 (br, 2H), 3.76-3.86 (m, 3H); ^{13}C NMR δ -5.5 (CH_3), 18.3 (C), 25.8 (CH_3), 45.6 (CH), 64.8 (CH_2), 120.8 (C). Anal. Calc. For $C_9H_{20}N_2OSi$: C, 53.95; H, 10.06; N, 13.98. Found: C, 53.78; H, 10.21; N, 13.72.

(2*S*,3*R*)-2-Amino-3-[(*tert*-butyldimethylsilyl)oxy]-butanenitrile (15b).[7] Prepared according to General Procedure B. Protected compound **14b** (10.00 g, 31.8 mmol) afforded the α-aminonitrile as a colorless oil (3.51 g, 51%): ^{1}H NMR δ 0.11 (s, 3H), 0.13 (s, 3H), 0.90 (s, 9H), 1.26-1.28 (d, 3H, J = 6.3 Hz), 1.54-1.66 (br, 2H), 3.51-3.64 (br, 1H), 3.98-4.06 (m, 1H); ^{13}C NMR δ -4.9 (CH_3), -4.5 (CH_3), 17.9 (C), 19.6 (CH_3), 25.7 (CH_3), 50.2 (CH), 69.4 (CH), 121.0 (C). Anal. Calc. For $C_{10}H_{22}N_2OSi$: C, 56.03; H, 10.34; N, 13.07. Found: C, 55.66; H, 10.52; N, 12.99.

(*S)*-2-Amino-3-phenylpropanenitrile (17).[8] Prepared according to General Procedures A and B from the known[9] (*S*)-2-[(*tert*-butoxycarbonyl)amino]-3-phenylpropionamide. The desired α-aminonitrile was obtained as a white solid (8.55 g, 72% from the amide): mp 60-61 °C; ^{1}H NMR δ 1.57-1.66 (br, 2H), 3.03-3.05 (d, 2H, J = 6.3 Hz), 3.93-3.97 (t, 1H, J = 6.3 Hz), 7.26-7.60 (m, 5H); ^{13}C NMR δ 41.1 (CH_2),

44.7 (CH), 121.6 (C), 127.7 (CH), 128.9 (CH), 129.6 (CH), 134.9 (C). Anal. Calc. For $C_9H_{10}N_2$: C, 73.94; H, 6.89; N, 19.16. Found: C, 73.71; H, 6.86; N, 19.12.

(*S*)-Methyl 2-[(*tert*-butoxycarbonyl)amino]-4-azido-butanoate (21). Acetyl chloride (35.0 mL, 0.49 mol, 1000 mol%) was added dropwise to anhydrous MeOH (260 mL) at 0 °C. Upon completion of the addition, the mixture was allowed to warm to room temperature and was stirred for 30 min before the carboxylic acid **20** (12.95 g, 49.2 mmol) was added as a solid. The mixture was then stirred for a further 24 h before the solvent was evaporated to afford the methyl ester as an off-white solid (12.8 g, 94%). Analytical data were in agreement with those previously published:[10] mp 128-130 ºC; ^{1}H NMR δ (CD_3OD) 2.30-2.39 (m, 1H), 2.41-2.57 (m, 1H), 3.58-3.63 (t, 2H, J = 6.8 Hz), 3.85 (s, 3H), 4.20-4.24 (t, 1H, J = 6.4 Hz), 4.86-4.91 (br, 3H).

A mixture of the methyl ester prepared above (11.70 g, 42.2 mmol), di-*tert*-butyl dicarbonate (9.68 g, 44.4 mmol, 105 mol%) and 1,4-dioxane (80 mL) was cooled to 0 °C. To this mixture was added, dropwise, a solution of $NaHCO_3$ (14.20 g, 0.169 mol, 400 mol%) in water (80 mL) (slow addition of the base minimized formation of an azetidine side-product) and the mixture was stirred at 0 °C for a further 16 h. After this time, the mixture was diluted with water (200 mL) then extracted with CH_2Cl_2 (3 × 200 mL). The combined organic phase was dried, filtered and concentrated to leave a crude brown oil. This oil was purified by column chromatography using a 10-30% EtOAc/hexanes gradient as the eluent. Evaporation of the solvent afforded the *N*-protected compound as a colorless oil (12.30 g, 98%). Analytical data were in agreement with those previously published:[11] ^{1}H NMR δ 1.43 (s, 9H), 2.08-2.25 (m, 1H), 2.36-2.43 (m, 1H), 3.40-3.44 (t, 1H, J = 7.2 Hz), 3.69 (s, 3H), 4.45-4.56 (br, 1H), 5.07-5.18 (br, 1H).

To a solution of the *N*-protected compound prepared above (5.90 g, 19.9 mmol) in acetone (200 mL) was added sodium iodide (5.97 g, 39.8 mmol, 200 mol%) and the mixture was heated under reflux for 2 h. After this time, the mixture was filtered and then concentrated to leave a crude yellow oil. This oil was purified by column chromatography using 10% EtOAc/hexanes as the eluent. Evaporation of the solvent afforded the iodide as a pale yellow oil (6.15 g, 90%). Analytical data were in agreement with

those previously published:[11] ^{1}H NMR δ 1.43 (s, 9H), 2.08-2.21 (m, 1H), 2.29-2.47 (m, 1H), 3.13-3.18 (t, 1H, *J* = 7.8 Hz), 3.74 (s, 3H), 4.28-4.37 (br, 1H), 5.09-5.15 (br, 1H).

A mixture of the iodide (6.10 g, 17.8 mmol), sodium azide (2.00 g, 30.8 mmol, 170 mol%) in anhydrous DMF (100 mL) was heated at 90 °C for 2 h. After this time, the solvent was evaporated to leave a yellow, semi-solid residue, which was partitioned between brine (100 mL) and EtOAc (3 × 100 mL). The combined organic phase was dried, filtered and then concentrated to leave a crude yellow oil. This oil was purified by column chromatography using 10% EtOAc/hexanes as the eluent. Evaporation of the solvent afforded the azide as a colorless oil (4.45 g, 97%): ^{1}H NMR δ 1.44 (s, 9H), 1.86-1.98 (m, 1H), 2.04-2.16 (m, 1H), 3.38-3.43 (t, 2H, *J* = 6.9 Hz), 3.77 (s, 3H), 4.36-4.46 (m, 1H) and 5.11-5.23 (m, 1H); ^{13}C NMR δ 28.2 (CH_3), 31.8 (CH_2), 47.7 (CH), 51.2 (CH_2), 52.6 (CH_3), 80.2 (C), 155.3 (C), 172.5 (C). Anal. Calc. For $C_{10}H_{18}N_4O_4$: C, 46.50; H, 7.03; N, 21.69. Found: C, 46.39; H, 7.07; N, 21.84.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-4-azido-butyramide (22). In a glass pressure tube, a solution of methyl ester **21** (193 mg, 0.75 mmol) in anhydrous MeOH (10 mL) was cooled to 0 °C and then saturated with ammonia gas. The tube was then sealed and the stirred mixture was heated at 50 °C for 24 h. After this time, the solvent was evaporated to afford the primary amide as a white solid requiring no further purification (182 mg, 99%): mp 95-96 °C; ^{1}H NMR δ 1.46 (s, 9H), 1.91-2.05 (m, 1H), 2.11-2.18 (m, 1H), 3.43-3.48 (t, 2H, *J* = 6.6 Hz), 4.37-4.46 (m, 1H), 5.22-5.24 (d, 1H, *J* = 7.5 Hz) and 5.30-5.80 (br, 2H); ^{13}C NMR δ 28.3 (CH_3), 31.7 (CH_2), 48.1 (CH), 51.7 (CH_2), 80.4 (C), 155.8 (C), 174.3 (C). Anal. Calc. For $C_9H_{17}N_5O_3$: C, 44.43; H, 7.04; N, 28.79. Found: C, 44.30; H, 7.05; N, 29.00.

(*S*)-2-[(*tert*-Butoxycarbonyl)amino]-4-azido-butanenitrile (23). Prepared according to General Procedure A. Primary amide **22** (19.6 g, 80.6 mmol) afforded the nitrile as a white solid (18.0 g, 99%): mp 74-75 °C; ^{1}H NMR δ 1.47 (s, 9H), 1.98-2.13 (dt, 2H, *J* = 12.7, 6.4 Hz), 3.52-3.74 (dt, 2H, *J* = 1.9, 6.4 Hz), 4.69-4.76 (br, 1H) and 5.07-5.16 (br, 1H); ^{13}C NMR δ 28.2 (CH_3), 32.2 (CH_2), 40.2 (CH), 47.3 (CH_2), 81.4 (C), 118.2 (C), 154.4 (C). Anal. Calc. For $C_9H_{15}N_5O_2$: C, 47.99; H, 6.71; N, 31.09. Found: C, 48.00; H, 6.73; N, 31.37.

(*S*)-2-Amino-4-azido-butanenitrile (24). Prepared according to General Procedure B. Protected compound **23** (4.00 g, 17.8 mmol) afforded the α-aminonitrile as a colorless oil (1.64 g, 74%): ^{1}H NMR δ 1.58-1.69 (br, 2H), 1.89-2.07 (m, 2H), 3.49-3.68 (m, 2H), 3.79-3.88 (br, 1H); ^{13}C NMR δ 34.3 (CH_2), 40.7 (CH), 47.3 (CH_2), 121.6 (C). Anal. Calc. For $C_4H_7N_5$: C, 38.39; H, 5.64; N, 55.97. Found: C, 38.44; H, 6.00; N, 55.61.

General Procedure C. Phase-transfer Alkylation of 2-[(Diphenylmethylene)amino]acetonitrile 26. To a solution of 2-[(diphenylmethylene)amino]acetonitrile **26** (100 mol%) in CH_2Cl_2 (0.6 M) was added the alkyl halide (105 mol%), 11 M aq. NaOH (1800 mol%) and then benzyltriethylammonium chloride (10 mol%). The resultant two-phase mixture was stirred vigorously until complete reaction as judged by TLC. The mixture was then diluted with water and extracted with CH_2Cl_2. The organic phase was dried, filtered and concentrated to leave a crude product, which was purified by column chromatography using an EtOAc/hexanes gradient containing 1% Et_3N.

2-[(Diphenylmethylene)amino]-3-(4-methoxyphenyl)propanenitrile (27a). Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (6.84 g, 31.0 mmol) the alkylated product was obtained as a yellow oil (8.70 g, 82%): ^{1}H NMR δ 3.13-3.28 (m, 2H), 3.81 (s, 3H), 4.36-4.41 (t, 1H, J = 7.2 Hz), 6.80-6.83 (d, 2H, J = 8.7 Hz), 6.87-6.90 (m, 2H), 7.03-7.06 (d, 2H, J = 8.7 Hz), 7.38-7.48 (m, 6H), 7.63-7.67 (d, 2H, J = 8.1 Hz); ^{13}C NMR δ 40.3 (CH_2), 55.2 (CH), 55.3 (CH_3), 113.9 (CH), 119.4 (C), 127.3 (CH), 127.6 (C), 128.3 (CH), 128.8 (CH), 129.0 (CH), 130.8 (CH), 131.2 (CH), 135.1 (C), 138.4 (C), 158.8 (C), 173.2 (C). Anal. Calc. For $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 80.99, H, 5.99; N, 8.19.

2-[(Diphenylmethylene)amino]-3-(4-nitrophenyl)propanenitrile (27b). Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (6.84 g, 31.0 mmol) the alkylated product was obtained as a yellow oil (10.26 g, 93%): ^{1}H NMR δ 3.32-3.35 (d, 2H, J = 9.0 Hz), 4.44-4.49 (t, 1H, J = 9.0 Hz), 6.92-6.94 (d, 2H, J = 6.0 Hz), 7.31-7.38 (m, 4H), 7.45-7.50 (m, 4H), 7.59-7.62 (d, 2H, J = 9.0 Hz), 8.14-8.17 (d, 2H, J = 9.0 Hz); ^{13}C NMR δ 40.7 (CH_2), 53.9 (CH), 118.6 (C), 123.7 (CH), 127.1 (CH), 128.4 (CH), 129.0 (CH), 129.1 (CH), 129.6 (CH), 130.7 (CH), 131.6 (CH), 134.8 (C), 137.9 (C), 143.1 (C), 146.9

(C), 174.0 (C). Anal. Calc. For $C_{22}H_{17}N_3O_2$: C, 74.35; H, 4.82; N, 11.82. Found: C, 74.22, H, 5.04; N, 11.70.

2-[(Diphenylmethylene)amino]octanenitrile (27c). Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (6.84 g, 31.0 mmol) the alkylated product was obtained as a yellow oil (8.29 g, 88%): ^{1}H NMR δ 0.91–0.96 (t, 3H, *J* = 7.2 Hz), 1.31-1.35 (m, 6H), 1.48 (m, 2H), 1.99-2.03 (m, 2H, *J* = 7.2 Hz), 4.26-4.31 (t, 1H, *J* = 6.6 Hz), 7.27-7.30 (m, 2H), 7.43-7.48 (m, 2H), 7.54-7.73 (m, 4H), 7.87-7.90 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR δ 14.0 (CH_3), 22.5 (CH_2), 25.5 (CH_2), 28.6 (CH_2), 31.5 (CH_2), 34.9 (CH_2), 53.1 (CH), 119.8 (C), 127.4 (CH), 128.2 (CH), 129.0 (CH), 130.1 (CH), 131.1 (CH), 132.4 (CH), 135.3 (C), 137.6 (C), 173.6 (C). Anal. Calc. For $C_{21}H_{24}N_2$: C, 82.85; H, 7.95; N, 9.20. Found: C, 83.18, H, 7.59; N, 8.84.

2-[(Diphenylmethylene)amino]-3-methylbutanenitrile (27d).[12] Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (6.84 g, 31.0 mmol) the alkylated product was obtained as a yellow oil (6.78 g, 83%): ^{1}H NMR δ 1.01-1.03 (d, 3H, *J* = 6.9 Hz), 1.13-1.14 (d, 3H, *J* = 6.6 Hz), 2.12-2.19 (m, 1H), 3.98-4.00 (d, 1H, *J* = 6.3 Hz), 7.21-7.25 (m, 2H), 7.27-7.32 (m, 2H), 7.33-7.55 (m, 4H), 7.63-7.66 (d, 2H, *J* = 8.1 Hz); ^{13}C NMR δ 18.6 (CH_3), 19.0 (CH_3), 33.6 (CH) 59.5 (CH), 119.0 (C), 127.3, 128.3, 129.0, 129.7, 131.1 (CH), 132.5 (CH), 135.4 (C), 137.6 (C), 173.0 (C). Anal. Calc. For $C_{18}H_{18}N_2$: C, 82.41; H, 6.92; N, 10.68. Found: C, 82.53; H, 6.89; N, 10.48.

Ethyl 4-cyano-4-[(diphenylmethylene)amino]butanoate (27e). Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (13.68 g, 62.1 mmol) the alkylated product was obtained as a yellow oil (19.68 g, 99%): ^{1}H NMR δ 1.23-1.28 (t, 3H, *J* = 7.2 Hz), 2.20-2.30 (m, 2H), 2.41-2.64 (m, 2H), 4.00-4.08 (q, 2H, *J* = 7.2 Hz), 4.32-4.36 (t, 1H, *J* = 6.3 Hz), 7.20-7.22 (m, 2H), 7.29-7.36 (m, 2H), 7.38-7.54 (m, 4H), 7.59-7.69 (m, 2H); ^{13}C NMR δ 14.1 (CH_3), 29.9 (CH_2), 30.0 (CH_2), 51.9 (CH), 60.7 (CH_2), 119.4 (C), 127.3 (CH), 128.2 (CH), 129.1 (CH), 129.5 (CH), 130.1 (CH), 131.3 (CH), 135.1 (C), 138.3 (C), 172.1 (C), 178.0 (C). Anal. Calc. For $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.67, H, 6.50; N, 8.36.

Ethyl 5-cyano-5-[(diphenylmethylene)amino]pentanoate (27f). Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (13.68 g, 62.1 mmol) the alkylated product was obtained as a yellow oil (19.64 g, 95%): ^{1}H NMR δ 1.22-1.27 (t, 3H, *J* = 7.2 Hz), 1.71-1.81 (m, 2H), 1.87-2.03 (m, 2H), 2.28-2.33 (t, 2H, *J* = 7.2 Hz), 4.08-4.15 (q, 2H, *J* = 7.2 Hz), 4.21-4.25 (t, 1H, *J* = 7.2 Hz), 7.20-7.23 (m, 2H), 7.33-7.38 (m, 2H), 7.42-7.54 (m, 4H), 7.63-7.66 (d, 2H, *J* = 7.2 Hz); ^{13}C NMR δ 14.2 (CH_3), 21.0 (CH_2), 33.5 (CH_2), 34.2 (CH_2), 52.7 (CH), 60.5 (CH_2), 119.4 (C), 127.4 (CH), 128.3 (CH), 128.9 (CH), 129.1 (CH), 129.4 (CH), 131.2 (CH), 135.2 (C), 138.4 (C), 172.9 (C), 173.2 (C). Anal. Calc. For $C_{21}H_{22}N_2O_2$: C, 75.42; H, 6.63; N, 8.38. Found: C, 75.65, H, 6.89; N, 8.35.

2-[(Diphenylmethylene)amino]-5-chloropentanenitrile (27g). Starting with 2-[(diphenylmethylene)amino]acetonitrile **26** (0.684 g, 3.1 mmol) the alkylated product was obtained as a yellow oil (0.843 g, 92%): ^{1}H NMR δ 1.89-2.14 (m, 4H), 3.53-3.59 (t, 2H, *J* = 6.6 Hz), 4.26-4.30 (t, 1H, *J* = 6.0 Hz), 7.20-7.23 (m, 2H), 7.33-7.39 (m, 2H), 7.41-7.57 (m, 4H) and 7.63-7.66 (m, 2H); ^{13}C NMR δ 28.5 (CH_2), 32.2 (CH_2), 44.2 (CH_2), 52.4 (CH), 119.3 (C), 127.4 (CH), 128.3 (CH), 129.1 (CH), 129.2 (CH), 129.5 (CH), 131.4 (CH), 135.1 (C), 138.3 (C), 173.4 (C). Anal. Calc. For $C_{18}H_{17}N_2Cl$: C, 72.84; H, 5.77; N, 9.44. Found: C, 72.85, H, 5.91; N, 9.20.

2-[(Diphenylmethylene)amino]-5-azidopentanenitrile (27h). To a solution of alkyl chloride **63** (650 mg, 2.19 mmol) in anhydrous DMF (10 mL) was added sodium azide (285 mg, 4.38 mmol, 200 mol%) and the mixture was then heated at 80 °C for 24 h. After this time, the solvent was evaporated to leave a yellow, semi-solid residue. This residue was partitioned between Et_2O (40 mL) and water (10 mL). The separated organic phase was then washed with more water (10 mL), then brine (10 mL) before it was dried, filtered and concentrated to leave a yellow oil. This oil was purified by column chromatography using 10%EtOAc/hexanes containing 1% Et_3N as the eluent. Evaporation of the solvent afforded the azide as a yellow oil (635 mg, 95%): ^{1}H NMR δ 1.69-1.83 (m, 2H), 1.93-2.09 (m, 2H), 3.30-3.34 (t, 2H, *J* = 6.7 Hz), 4.26-4.30 (t, 1H, *J* = 6.4 Hz), 7.20-7.23 (m, 2H), 7.33-7.39 (m, 2H), 7.41-7.55 (m, 4H) and 7.63-7.66 (m, 2H); ^{13}C NMR δ 28.5 (CH_2), 32.2 (CH_2), 44.2 (CH_2), 52.4 (CH), 119.3 (C), 127.4 (CH),

128.3 (CH), 129.1 (CH), 129.2 (CH), 129.5 (CH), 131.4 (CH), 135.1 (C), 138.3 (C), 173.4 (C). Anal. Calc. For $C_{18}H_{17}N_5$: C, 71.27; H, 5.65; N, 23.09. Found: C, 71.35, H, 5.79; N, 22.99.

General Procedure D. Hydrolysis of Alkylated Benzophenone Imines. To a solution of the imine (100 mol%) in THF (0.25 M) was added 1 M aq. HCl (105 mol%) over a 1 h period using a syringe pump. After complete reaction as judged by TLC, sat. aq. $NaHCO_3$ was added and then the THF was evaporated. The residue was partitioned between dil. aq. NH_4OH and CH_2Cl_2. The organic phase was dried, filtered and concentrated to leave a crude product, which was purified by column chromatography using an EtOAc/hexanes gradient containing 1% Et_3N as the eluent. Evaporation of the solvent afforded the α-aminonitriles.

2-Amino-3-(4-methoxyphenyl)propanenitrile (28a). Imine **27a** (8.70 g, 25.6 mmol) afforded the α-aminonitrile as a colorless oil (3.91 g, 87%): ^{1}H NMR δ 1.53-1.62 (br, 2H), 2.96-2.99 (dd, 2H, J = 6.0, 2.1 Hz), 3.80 (s, 3H), 3.83-3.94 (br, 1H), 6.88-6.91 (d, 2H, J = 8.7 Hz), 7.20-7.23 (d, 2H, J = 8.7 Hz); ^{13}C NMR δ 40.2 (CH_2), 44.8 (CH), 55.3 (CH_3), 114.2 (CH), 121.7 (C), 126.8 (C), 130.7 (CH), 159.1 (C). Anal. Calc. For $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 67.94, H, 6.94; N, 15.86.

2-Amino-3-(4-nitrophenyl)propanenitrile (28b). Imine **27b** (8.00 g, 22.5 mmol) afforded the α-aminonitrile as a yellow solid (3.84 g, 89%): mp 81-82 °C; ^{1}H NMR δ 1.66-1.69 (d, 2H, J = 7.5 Hz), 3.13-3.16 (dd, 2H, J = 6.3, 1.5 Hz), 3.94-4.04 (m, 1H), 7.48-7.51 (d, 2H, J = 8.7 Hz), 8.22-8.25 (d, 2H, J = 8.7 Hz); ^{13}C NMR δ 40.9 (CH_2), 44.2 (CH), 120.9 (C), 124.0 (CH), 130.6 (CH), 142.4 (C), 147.5 (C). Anal. Calc. For $C_9H_9N_3O_2$: C, 56.54; H, 4.74; N, 21.98. Found: C, 56.50, H, 4.75; N, 22.07.

2-Aminooctanenitrile (28c).[29] Imine **27c** (6.85 g, 22.5 mmol) afforded the α-aminonitrile as a colorless oil (2.97 g, 94%): ^{1}H NMR δ 0.87-0.91 (t, 3H, J = 6.6 Hz), 1.24-1.42 (m, 6H), 1.43-1.55 (m, 2H), 1.56-1.67 (m, 2H), 1.70-1.78 (m, 2H), 3.61-3.72 (br, 1H); ^{13}C NMR δ 13.9 (CH_3), 22.4 (CH_2), 25.3 (CH_2), 28.6 (CH_2), 31.5 (CH_2), 35.2 (CH_2), 43.3 (CH), 122.4 (C). Anal. Calc. For $C_8H_{16}N_2$: C, 68.52; H, 11.50; N, 19.98. Found: C, 68.28, H, 11.18; N, 19.62.

2-Amino-3-methylbutanenitrile (28d). Imine **27d** (6.35 g, 24.2 mmol) afforded the α-aminonitrile as a colorless oil (2.18 g, 92%): ^{1}H NMR δ 1.06-1.07 (d, 3H, *J* = 2.7 Hz), 1.09-1.10 (d, 3H, *J* = 2.7 Hz), 1.76-1.86 (br, 2H), 1.87-2.02 (m, 1H), 3.53-3.55 (d, 1H, *J* = 5.7 Hz); ^{13}C NMR δ 17.5 (CH_3), 18.8 (CH_3), 32.8 (CH), 49.7 (CH), 121.3 (C). Anal. Calc. For $C_5H_{10}N_2$: C, 61.19; H, 10.27; N, 28.54. Found: C, 61.35, H, 10.07; N, 28.32.

Ethyl 4-amino-4-cyanobutanoate (28e). Imine **27e** (19.90 g, 62.1 mmol) afforded the α-aminonitrile as a colorless oil (7.50 g, 77%): ^{1}H NMR δ 1.24-1.29 (t, 3H, *J* = 7.2 Hz), 1.69-1.80 (br, 2H), 2.03-2.10 (q, 2H, *J* = 7.1 Hz), 2.51-2.58 (m, 2H), 3.80-3.84 (t, 1H, *J* = 7.1 Hz), 4.11-4.18 (q, 2H, *J* = 7.2 Hz); ^{13}C NMR δ 14.1 (CH_3), 29.9 (CH_2), 30.2 (CH_2), 42.5 (CH), 60.8 (CH_2), 121.8 (C), 172.3 (C). Anal. Calc. For $C_7H_{12}N_2O_2$: C, 53.83; H, 7.74; N, 17.94. Found: C, 53.77, H, 7.75; N, 17.65.

Ethyl 5-amino-5-cyanopentanoate (28f). Imine **27f** (8.40 g, 25.1 mmol) afforded the α-aminonitrile as a colorless oil (3.33 g, 78%): ^{1}H NMR δ 1.23-1.28 (t, 3H, *J* = 6.9 Hz), 1.81-1.84 (m, 4H), 2.25-2.31 (br, 2H), 2.34-2.40 (m, 2H), 3.74-3.78 (t, 1H, *J* = 6.6 Hz), 4.10-4.17 (q, 2H, *J* = 6.9 Hz); ^{13}C NMR δ 14.2 (CH_3), 20.8 (CH_2), 33.4 (CH_2), 34.6 (CH_2), 43.1 (CH), 60.5 (CH_2), 122.0 (C), 172.8 (C). Anal. Calc. For $C_8H_{14}N_2O_2$: C, 56.45; H, 8.29; N, 16.46. Found: C, 56.49, H, 8.24; N, 16.25.

2-Amino-5-azidopentanenitrile (28g). Imine **27h** (245 mg, 0.81 mmol) afforded the α-aminonitrile as a colorless oil (90 mg, 80%): ^{1}H NMR δ 1.52-1.69 (br, 2H), 1.74-1.89 (m, 4H), 3.36-3.40 (t, 2H, *J* = 6.3 Hz), 3.64-3.77 (br, 1H); ^{13}C NMR δ 25.0 (CH_2), 32.5 (CH_2), 42.9 (CH), 50.6 (CH_2), 122.0 (C). Anal. Calc. For $C_5H_9N_5$: C, 43.15; H, 6.52; N, 50.33. Found: C, 43.64, H, 6.76; N, 49.94.

General Procedure E. Conversion α-Aminonitriles to Methyl Imidates. To a solution of the α-aminonitrile (100 mol%) in trimethylorthoformate (0.1 M) was added PPTS (0.2 mol%) and the mixture was heated at 65 °C for 1 h. The mixture was then concentrated to afford microanalytically pure methyl imidate, normally as a colorless oil, in near quantitative yield.

2-[(Methoxymethylene)amino]-3-phenylpropanenitrile (29a). α-Aminonitrile **17** (292 mg, 2.00 mmol) gave the imidate as a colorless oil (374 mg, 99%): ^{1}H NMR δ 3.10-3.12 (d, 2H, *J* = 6.6 Hz), 3.74

(s, 3H), 4.41-4.46 (t, 1H, J = 6.6 Hz), 7.21-7.36 (m, 5H), 7.54 (s, 1H); ^{13}C NMR δ 41.5 (CH_2), 53.5 (CH), 54.0 (CH_3), 118.7 (C), 127.5 (C), 128.6 (CH), 129.8 (CH), 135.2 (CH), 158.7 (CH). Anal. Calc. For $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.21; H, 6.10; N, 15.04.

2-[(Methoxymethylene)amino]-3-azidopropanenitrile (29b). α-Aminonitrile **12** (222 mg, 2.00 mmol) gave the imidate as a colorless oil (306 mg, 99%): ^{1}H NMR δ 3.57-3.59 (d, 2H, J = 5.7 Hz), 3.79 (s, 3H), 4.42-4.46 (dt, 1H, J = 5.7, 0.9 Hz), 7.85 (s, 1H). This compound was too unstable for further characterization and was used directly in the attempted preparation of the imidazole.

2-[(Methoxymethylene)amino]-3-[(*tert*-butyldimethylsilyl)oxy]propanenitrile (29c). α-Aminonitrile **15a** (401 mg, 2.00 mmol) gave the imidate as a colorless oil (484 mg, 99%): ^{1}H NMR δ 0.08 (s, 6H), 0.89 (s, 9H), 3.74 (s, 3H), 3.81-3.83 (d, 2H, J = 6.0 Hz), 4.31-4.34 (t, 1H, J = 6.0 Hz), 7.76 (s, 1H); ^{13}C NMR δ -5.4 (CH_3), -5.3 (C), 18.2 (C), 25.7 (CH_3), 53.9 (CH_3), 54.2 (CH), 64.4 (CH_2), 117.9 (C), 159.5 (CH). Anal. Calc. For $C_{11}H_{22}N_2O_2Si$: C, 54.51; H, 9.15; N, 11.56. Found: C, 54.28; H, 9.11; N, 11.64.

2-[(Methoxymethylene)amino]-3-[(*tert*-butyldimethylsilyl)oxy]butanenitrile (29d). α-Aminonitrile **15b** (429 mg, 2.00 mmol) gave the imidate as a colorless oil (513 mg, 99%): ^{1}H NMR δ 0.06 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 1.28-1.30 (d, 3H, J = 6.3 Hz), 3.74 (s, 3H), 3.95-4.03 (m, 1H), 4.13-4.15 (dd, 1H, J = 6.0, 0.6 Hz), 7.70 (s, 1H); ^{13}C NMR δ –4.9 (CH_3), -4.6 (CH_3), 17.9 (C), 19.7 (CH_3), 25.6 (CH_3), 53.9 (C), 59.5 (CH), 69.3 (CH), 117.8 (C), 159.2 (CH). Anal. Calc. For $C_{12}H_{24}N_2O_2Si$: C, 56.21; H, 9.43; N, 10.92. Found: C, 55.94; H, 9.23; N, 11.09.

2-[(Methoxymethylene)amino]-4-azidobutanenitrile (29e). α-Aminonitrile **24** (250 mg, 2.00 mmol) gave the imidate as a colorless oil (333 mg, 99%): ^{1}H NMR δ 1.98-2.16 (m, 2H), 3.42-3.54 (m, 2H), 3.76 (s, 3H), 4.39-4.43 (t, 1H, J = 6.6 Hz), 7.80 (s, 1H); ^{13}C NMR δ 34.4 (CH_2), 47.0 (CH_2), 48.6 (CH), 54.8 (CH_3), 118.5 (C), 159.2 (CH). Anal. Calc. For $C_6H_9N_5O$: C, 43.11; H, 5.43; N, 41.89. Found: C, 42.89; H, 5.61; N, 41.79.

2-[(Methoxymethylene)amino]-3-(4-methoxyphenyl)propanenitrile (29f). α-Aminonitrile **28a** (352 mg, 2.00 mmol) gave the imidate as a colorless oil (432 mg, 99%): ^{1}H NMR δ 3.04-3.06 (d, 2H, *J* = 6.9 Hz), 3.75 (s, 3H), 3.78 (s, 3H), 4.37-4.41 (t, 1H, *J* = 6.9 Hz), 6.84-6.87 (d, 2H, *J* = 8.7 Hz), 7.13-7.16 (d, 2H, *J* = 8.7 Hz), 7.53 (s, 1H); ^{13}C NMR δ 40.6 (CH_2), 53.7 (CH), 54.0 (CH_3), 55.2 (CH_3), 114.0 (CH), 118.8 (C), 127.2 (C), 130.8 (CH),158.7 (C), 158.9 (CH). Anal. Calc. For $C_{12}H_{14}N_2O_2$: C, 66.04; H, 6.47; N, 12.84. Found: C, 66.29; H, 6.55; N, 13.10.

2-[(Methoxymethylene)amino]-3-(4-nitrophenyl)propanenitrile (29g). α-Aminonitrile **28b** (382 mg, 2.00 mmol) gave the imidate as a colorless oil (466 mg, 99%): ^{1}H NMR δ 3.21-3.23 (d, 2H, *J* = 6.6 Hz), 3.73 (s, 3H), 4.51-4.55 (t, 1H, *J* = 6.6 Hz), 7.41-7.44 (d, 2H, *J* = 8.7 Hz), 7.61 (s, 1H), 8.17-8.19 (d, 2H, *J* = 8.7 Hz); ^{13}C NMR δ 41.0 (CH_2), 52.4 (CH), 54.2 (CH_3), 117.9 (C), 123.7 (CH), 130.8 (CH), 142.7 (C), 147.4 (C), 159.1 (CH). Anal. Calc. For $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.02. Found: C, 56.70; H, 5.03; N, 17.83.

2-[(Methoxymethylene)amino]octanenitrile (29h). α-Aminonitrile **28c** (280 mg, 2.00 mmol) gave the imidate as a colorless oil (364 mg, 99%): ^{1}H NMR δ 0.86-0.91 (t, 3H, *J* = 6.6 Hz), 1.23-1.49 (m, 8H), 1.77-1.84 (m, 2H), 3.75 (s, 3H), 4.21-4.26 (t, 1H, *J* = 6.9 Hz), 7.76 (s, 1H); ^{13}C NMR δ 14.0 (CH_3), 22.5 (CH_2), 25.3 (CH_2), 28.6 (CH_2), 31.5 (CH_2), 35.4 (CH_2), 51.8 (CH), 53.9 (CH_3), 119.2 (C), 158.2 (CH). Anal. Calc. For $C_{10}H_{18}N_2O$: C, 65.90; H, 9.95; N,15.37. Found: C, 66.04; H, 9.84; N,15.42.

2-[(Methoxymethylene)amino]-3-methylbutanenitrile (29i). α-Aminonitrile **28d** (196 mg, 2.00 mmol) gave the imidate as a colorless oil (214 mg, 76%): ^{1}H NMR δ 1.02-1.04 (d, 3H, *J* = 3.9 Hz), 1.05-1.06 (d, 3H, *J* = 3.9 Hz), 1.97-2.12 (m, 1H), 3.75 (s, 3H), 4.07-4.10 (d, 1H, *J* = 5.7 Hz), 7.74 (s, 1H). This compound was too volatile/unstable for further characterization.

Ethyl 4-cyano-4-[(methoxymethylene)amino]butanoate (29j). α-Aminonitrile **28e** (312 mg, 2.00 mmol) gave the imidate as a colorless oil (395 mg, 99%): ^{1}H NMR δ 1.24-1.29 (t, 3H, *J* = 7.2 Hz), 2.05-2.22 (m, 2H), 2.48-2.53 (t, 2H, *J* = 7.1 Hz), 3.74 (s, 3H), 4.11-4.17 (q, 2H, *J* = 7.2 Hz), 4.38-4.43 (t, 1H, *J* = 7.1 Hz), 8.07 (s, 1H); ^{13}C NMR δ 14.1 (CH_3), 29.6 (CH_2), 30.4 (CH_2), 50.5 (CH), 53.9 (C), 60.7

(CH_2), 118.6 (C), 158.8 (CH), 172.2 (C). Anal. Calc. For $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.59; H, 6.99; N, 14.41.

Ethyl 5-cyano-5-[(methoxymethylene)amino]pentanoate (29k). α-Aminonitrile **28f** (340 mg, 2.00 mmol) gave the imidate as a colorless oil (424 mg, 99%): ^{1}H NMR δ 1.23-1.28 (t, 3H, *J* = 7.2 Hz), 1.73-1.90 (m, 4H), 2.35-2.39 (t, 2H, *J* = 6.9 Hz), 3.74 (s, 3H), 4.10-4.17 (q, 2H, *J* = 7.2 Hz), 4.25-4.29 (t, 1H, *J* = 6.3 Hz), 7.77 (s, 1H); ^{13}C NMR δ 14.2 (CH_3), 20.7 (CH_2), 33.4 (CH_2), 34.6 (CH_2), 51.3 (CH), 53.9 (CH_3), 60.4 (CH_2), 118.8 (C), 158.5 (CH), 172.8 (C). Anal. Calc. For $C_{10}H_{16}N_2O_3$: C, 56.59; H, 7.60; N, 13.20. Found: C, 56.48; H, 7.59; N, 13.12.

2-[(Methoxymethylene)amino]-5-azidopentanenitrile (29l). α-Aminonitrile **28g** (278 mg, 2.00 mmol) gave the imidate as a colorless oil (359 mg, 99%): ^{1}H NMR δ 1.72-1.84 (m, 2H), 1.87-1.96 (m, 2H), 3.36-3.40 (t, 2H, *J* = 6.6 Hz), 3.75 (s, 3H), 4.29-4.33 (dt, 1H, *J* = 6.3, 0.6 Hz), 7.78 (s, 1H); ^{13}C NMR δ 24.8 (CH_2), 32.6 (CH_2), 50.7 (CH_2), 51.1 (CH), 54.0 (CH_3), 118.7 (C), 158.5 (CH). Anal. Calc. For $C_7H_{11}N_5O$: C, 46.40; H, 6.12; N, 38.65. Found: C, 46.59; H, 6.23; N, 39.02.

General Procedure F. Cyclization of Imidates to 5-Aminoimidazoles and Derivatizations. To a solution of the imidate in anhydrous $CHCl_3$ (0.1 M) was added the amine (100 mol%) and PPTS (1 mol%). The mixture was then heated under reflux for 16 h before it was concentrated to afford the crude 5-aminoimidazoles that were usually > 95% pure as judged by ^{1}H NMR spectroscopy. The unstable crude 5-aminoimidazoles were then immediately derivatized (compound **30** was the only free aminoimidazole that was partially characterized) as either methyl imidates or *N, N*-dimethylamidines by heating in trimethylorthoformate (0.1 M) or *N, N*-dimethylformamide dimethylacetal (0.1 M) at 80 °C for 24 h.

1,4-Dibenzyl-5-aminoimidazole (30). The imidate **29a** (374 mg, 1.99 mmol) gave the crude 5-aminoimidazole (containing 5 mg PPTS cat.) as a cream solid (528 mg, 100%): mp 97-103 °C (dec.); ^{1}H NMR δ 2.49-2.57 (br, 2H), 3.90 (s, 2H), 5.00 (s, 2H), 7.10-7.12 (d, 2H, *J* = 6.3 Hz), 7.14-7.37 (m, 9H); ^{13}C NMR δ 33.5 (CH_2), 47.3 (CH_2), 126.0 (C), 126.8 (CH), 127.9 (CH), 128.5 (CH), 128.7 (CH), 129.0

(CH), 130.2 (C), 130.8 (CH) 131.7 (CH), 136.6 (C), 140.4 (C). This compound was too unstable for further characterization.

1,4-Dibenzyl-5-[((*N,N*-dimethylamino)methylene)amino]imidazole (31a). The aminoimidazoles was derivatized as the *N, N*-dimethylamidine, obtained as a brown oil (576 mg, 91% from the α-aminonitrile): ^{1}H NMR δ 2.79-2.87 (br, 6H), 3.90 (s, 2H), 5.00 (s, 2H), 7.12-7.19 (m, 4H), 7.22-7.33 (m, 8H); ^{13}C NMR δ 33.9 (CH_3), 34.1 (CH_2), 39.9 (CH_3), 47.1 (CH_2), 123.0 (C), 125.7 (CH), 127.4 (CH), 127.6 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 131.4 (CH), 137.7 (C), 137.9 (C), 142.2 (C), 154.5 (CH). Anal. Calc. For $C_{20}H_{22}N_4$: C, 75.44; H, 6.96; N, 17.60. Found: C, 75.16; H, 7.06; N, 17.65.

1-Propyl-4-benzyl-5-[((*N,N*-dimethylamino)methylene)amino]imidazole (31b). The aminoimidazole was derivatized as the *N, N*-dimethylamidine, obtained as a brown solid (481 mg, 89% from the α-aminonitrile): mp 57-58 °C; ^{1}H NMR δ 0.88-0.91 (t, 3H, J = 7.5 Hz), 1.66-1.78 (m, 2H), 2.87 (br, 6H), 3.71-3.76 (t, 2H, J = 6.9 Hz), 3.87 (s, 2H), 7.10-7.17 (m, 2H), 7.22-7.28 (m, 5H); ^{13}C NMR δ 11.3 (CH_3), 23.8 (CH_2), 33.9 (CH_3), 34.0 (CH_2), 39.9 (CH_3), 45.3 (CH_2), 122.9 (C), 125.6 (CH), 128.3 (CH), 128.4 (CH), 131.2 (CH), 137.5 (C), 142.4 (C), 154.3 (CH). Anal. Calc. For $C_{16}H_{22}N_4$: C, 71.08; H, 8.20; N, 20.72. Found: C, 71.03; H, 8.29; N, 20.78.

1-Cyclopentyl-4-benzyl-5-[((*N,N*-dimethylamino)methylene)amino]imidazole (31c). The aminoimidazole was derivatized as the *N, N*-dimethylamidine, obtained as a brown solid (474 mg, 80% from the α-aminonitrile): mp 78-81 °C; ^{1}H NMR δ 1.61-1.85 (m, 6H), 2.10-2.12 (m, 2H), 2.85 (br, 6H), 3.84 (s, 2H), 4.41-4.50 (m, 1H), 7.09-7.16 (m, 2H), 7.23-7.28 (m, 5H); ^{13}C NMR δ 24.9 (CH_2), 33.0 (CH_2), 33.9 (CH_2), 34.1 (CH_2), 39.8 (CH_3), 55.0 (CH), 123.1 (C), 125.6 (CH), 128.3 (CH), 128.5 (CH), 128.8 (CH), 137.7 (C), 142.4 (C), 154.4 (CH). Anal. Calc. For $C_{18}H_{24}N_4$: C, 72.92; H, 8.16; N, 18.90. Found: C, 72.63; H, 8.39; N, 18.76.

1-Benzyl-4-[((*tert*-butyldimethylsilyl)oxy)methyl]-5-[((*N,N*-dimethylamino)methylene)-amino]imidazole (31d). The aminoimidazole was derivatized as the *N, N*-dimethylamidine, obtained as a yellow oil (320 mg, 43% from the α-aminonitrile): ^{1}H NMR δ 0.08 (s, 6H), 0.89 (s, 9H), 2.97 (s, 6H),

4.53 (s, 2H), 5.03 (s, 2H), 7.18-7.41 (m, 6H), 8.02 (s, 1H). ^{13}C NMR δ -4.9 (CH_3), 18.3 (C), 26.1 (CH_3), 33.9 (CH_3), 40.1 (CH_3), 46.9 (CH_2), 59.7 (CH_2), 123.3 (C), 127.4 (CH), 127.5 (CH), 128.5 (CH), 130.7 (CH), 137.8 (C), 140.2 (C), 155.6 (CH). Anal. Calc. For $C_{20}H_{32}N_4OSi$: C, 64.47; H, 8.66; N, 15.04. Found: C, 64.17; H, 8.82; N, 14.94.

1-Benzyl-4-(3-azidopropyl)-5-[((*N,N*-dimethylamino)methylene)amino]imidazole (31f). The aminoimidazole was derivatized as the *N, N*-dimethylamidine, obtained as a yellow oil (573 mg, 92% from the α-aminonitrile): ^{1}H NMR δ 1.93-2.02 (m, 2H), 2.56-2.61 (t, 2H, *J* = 7.2 Hz), 2.95 (s, 6H), 3.31-3.35 (t, 2H, *J* = 6.6 Hz), 4.97 (s, 2H), 7.14-7.17 (d, 2H, *J* = 6.8 Hz), 7.20-7.33 (m, 4H), 7.47 (s, 1H). ^{13}C NMR δ 24.1 (CH_2), 28.9 (CH_2), 34.0 (CH_3), 40.0 (CH_3), 47.0 (CH_2), 50.9 (CH_2), 122.8 (C), 127.4 (CH), 127.8 (CH), 128.6 (CH), 131.3 (CH), 137.3 (C), 137.9 (C), 154.3 (CH). Anal. Calc. For $C_{16}H_{21}N_7$: C, 61.71; H, 6.80; N, 31.49. Found: C, 61.56; H, 7.02; N, 31.73.

1,4-Dibenzyl-5-[(methoxymethylene)amino]imidazole (32a). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (550 mg, 90% from the α-aminonitrile): ^{1}H NMR δ 3.76 (s, 3H), 3.92 (s, 2H), 5.03 (s, 2H), 7.11-7.37 (m, 11H), 7.69 (s, 1H); ^{13}C NMR δ 33.8 (CH_2), 47.6 (CH_2), 53.6 (CH_3), 125.3 (C), 126.0 (CH), 127.3 (CH), 127.8 (CH), 128.4 (CH), 128.5 (CH), 128.8 (CH), 132.6 (C), 133.1 (CH), 137.1 (C), 140.7 (C), 156.5 (CH). Anal. Calc. For $C_{19}H_{19}N_3O$: C, 74.73; H, 6.27; N, 13.76. Found: C, 74.44; H, 6.29; N, 13.85.

1-Phenyl-4-benzyl-5-[(methoxymethylene)amino]imidazole (32b). The aminoimidazole was derivatized as the methyl imidate, obtained as a yellow oil (391 mg, 67% from the α-aminonitrile): ^{1}H NMR δ 3.73 (s, 3H), 3.96 (s, 2H), 7.16-7.23 (m, 1H), 7.29-7.31 (d, 4H, *J* = 4.5 Hz), 7.34-7.47 (m, 5H), 7.57 (s, 1H), 7.74 (s, 1H); ^{13}C NMR δ 32.9 (CH_2), 53.5 (CH_3), 125.7 (C), 126.1 (CH), 127.1 (CH), 127.6 (CH), 128.5 (CH), 128.7 (CH), 129.0 (CH), 132.4 (C), 133.3 (CH), 137.4 (C), 140.5 (C), 156.6 (CH). Anal. Calc. For $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found: C, 74.51; H, 6.02; N, 14.42.

1-Benzyl-4-(2-azidoethyl)-5-[((*N,N*-dimethylamino)methylene)amino]imidazole (32d). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (512 mg, 90% from the

α-aminonitrile): ^{1}H NMR δ 2.74-2.78 (t, 2H, *J* = 6.6 Hz), 3.62-3.67 (t, 2H, *J* = 6.6 Hz), 3.83 (s, 3H), 5.02 (s, 2H), 7.14-7.16 (d, 2H, *J* = 6.8 Hz), 7.27-7.35 (m, 4H), 7.98 (s, 1H); ^{13}C NMR δ 27.2 (CH_2), 47.5 (CH_2), 51.1 (CH_2), 53.7 (CH_3), 122.6 (C), 127.2 (CH), 127.8 (CH), 128.7 (CH), 133.3 (C), 133.5 (CH), 137.0 (C), 156.9 (CH). Anal. Calc. For $C_{14}H_{16}N_6O$: C, 59.14; H, 5.67; N, 29.56. Found: C, 59.00; H, 5.99; N, 29.91.

1-Benzyl-4-(4-methoxybenzyl)-5-[(methoxymethylene)amino]imidazole (32e). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (610 mg, 91% from the α-aminonitrile): ^{1}H NMR δ 3.76 (two overlapping s, 6H), 3.86 (s, 2H), 5.03 (s, 2H), 6.80-6.83 (d, 2H, *J* = 8.7 Hz), 7.11-7.18 (m, 4H), 7.27-7.36 (m, 4H), 7.71 (s, 1H); ^{13}C NMR δ 33.0 (CH_2), 47.5 (CH_2), 53.5 (CH_3), 55.2 (CH_3), 113.9 (CH), 125.7 (C), 127.3 (CH), 127.7 (CH), 128.7 (CH), 129.3 (CH), 132.4 (C), 132.8 (C), 133.1 (CH), 137.2 (C), 156.4 (CH), 157.9 (C). Anal. Calc. For $C_{20}H_{21}N_3O_2$: C, 71.62; H, 6.31; N, 12.53. Found: C, 71.34; H, 6.48; N, 12.52.

1-Benzyl-4-(4-nitrobenzyl)-5-[(methoxymethylene)amino]imidazole (32f). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown solid (651 mg, 93% from the α-aminonitrile): mp 69-70 °C; ^{1}H NMR δ 3.80 (s, 3H), 3.99 (s, 2H), 5.04 (s, 2H), 7.15-7.18 (d, 2H, *J* = 6.8 Hz), 7.29-7.40 (m, 6H), 7.67 (s, 1H), 8.12-8.15 (d, 2H, *J* = 8.7 Hz); ^{13}C NMR δ 33.5 (CH_2), 47.7 (CH_2), 53.8 (CH_3), 123.6 (C), 123.8 (CH), 127.3 (CH), 127.9 (CH), 128.8 (CH), 129.3 (CH), 133.1 (CH), 133.6 (C), 136.8 (C), 146.4 (C), 148.5 (C), 156.6 (CH). Anal. Calc. For $C_{19}H_{18}N_4O_3$: C, 65.13; H, 5.18; N, 15.99. Found: C, 65.08; H, 5.20; N, 15.97.

1-Benzyl-4-hexyl-5-[(methoxymethylene)amino]imidazole (32g). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (515 mg, 86% from the α-aminonitrile): ^{1}H NMR δ 0.85-0.89 (t, 3H, *J* = 6.6 Hz), 1.23-1.39 (m, 8H), 1.60-1.70 (m, 2H), 2.47-2.52 (t, 1H, *J* = 7.8 Hz), 3.82 (s, 2H), 5.01 (s, 2H), 7.14-7.16 (d, 2H, *J* = 6.8 Hz), 7.28-7.34 (m, 4H), 7.86 (s, 1H); ^{13}C NMR δ 14.1 (CH_3), 22.6 (CH_2), 27.5 (CH_2), 29.2 (CH_2), 29.9 (CH_2), 31.7 (CH_2), 47.5 (CH_2), 53.5 (CH_3),

127.2 (C), 127.3 (CH), 127.7 (CH), 128.7 (CH), 131.6 (C), 132.7 (CH), 137.2 (C), 156.0 (CH). Anal. Calc. For $C_{18}H_{25}N_3O$: C, 72.21; H, 8.42; N, 14.03. Found: C, 72.32; H, 8.44; N, 14.21.

1-Benzyl-4-(isopropyl)-5-[(methoxymethylene)amino]imidazole (32h). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (324 mg, 85% from imidate **29i**): ^{1}H NMR δ 1.22-1.24 (d, 6H, *J* = 6.9 Hz), 2.69-2.84 (sept, 1H, *J* = 6.9 Hz), 3.77 (s, 3H), 4.94 (s, 2H), 7.09-7.12 (m, 2H), 7.17-7.29 (m, 4H), 7.77 (s, 1H); ^{13}C NMR δ 23.0 (CH_3), 26.0 (CH), 47.4 (CH_2), 53.5 (CH_3), 127.2 (CH), 127.6 (CH), 128.7 (CH), 130.4 (C), 132.5 (C), 132.8 (CH), 137.2 (C), 156.3 (CH). Anal. Calc. For $C_{15}H_{19}N_3O$: C, 70.01; H, 7.44; N, 16.33. Found: C, 70.21; H, 7.58; N, 16.60.

Ethyl 3-[1-benzyl-5-((methoxymethylene)amino)imidazol-4-yl]propanoate (32i). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (530 mg, 84% from the α-aminonitrile): ^{1}H NMR δ 1.19-1.24 (t, 3H, *J* = 7.2 Hz), 2.72-2.86 (m, 4H), 3.83 (s, 3H), 4.07-4.14 (q, 2H, *J* = 7.2 Hz), 5.00 (s, 2H), 7.13-7.16 (d, 2H, *J* = 6.8 Hz), 7.28-7.34 (m, 4H), 8.03 (s, 1H); ^{13}C NMR δ 14.2 (CH_3), 22.4 (CH_2), 33.6 (CH_2), 47.4 (CH_2), 53.5 (CH_3), 60.3 (CH_2), 124.7 (C), 127.2 (CH), 127.7 (CH), 128.7 (CH), 132.1 (CH), 133.0 (CH), 137.1 (C), 156.9 (CH), 173.4 (C). Anal. Calc. For $C_{17}H_{21}N_3O_3$: C, 64.74; H, 6.71; N, 13.32. Found: C, 64.99; H, 6.84; N, 13.20.

Ethyl 4-[1-benzyl-5-((methoxymethylene)aminoimidazol-4-yl]butanoate (32j). The aminoimidazole was derivatized as the methyl imidate, obtained as a brown oil (534 mg, 81% from the α-aminonitrile): ^{1}H NMR δ 1.21-1.26 (t, 3H, *J* = 6.9 Hz), 1.93-2.03 (m, 2H, *J* = 7.2 Hz), 2.35-2.40 (t, 2H, *J* = 7.2 Hz), 2.54-2.58 (t, 2H, *J* = 7.2 Hz), 3.82 (s, 3H), 4.07-4.14 (q, 2H, *J* = 6.9 Hz), 5.01 (s, 2H), 7.14-7.16 (d, 2H, *J* = 6.9 Hz), 7.29-7.34 (m, 4H), 7.92 (s, 1H); ^{13}C NMR δ 14.2 (CH_3), 24.9 (CH_2), 26.6 (CH_2), 33.7 (CH_2), 47.4 (CH_2), 53.5 (CH_3), 60.2 (CH_2), 125.9 (C), 127.2 (CH), 127.7 (CH), 128.7 (CH), 132.0 (C), 132.9 (CH), 137.1 (C), 156.3 (CH), 173.6 (C). Anal. Calc. For $C_{18}H_{23}N_3O_3$: C, 65.63; H, 7.04; N, 12.76. Found: C, 65.40; H, 7.15; N, 12.66.

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