Preparation of *N*-Alkyl-bis(3-aminopropyl)amines by the Catalytic Hydrogenation of *N*-Alkyl-bis(cyanoethyl)amines

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SUPPORTING INFORMATION

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1. General Methods, Instrument Details and Materials. All chemicals, catalysts and solvents were purchased from commercial sources and were used without further purification. **Caution: Hydrogenations were carried out in a 500 mL flask using an all stainless steel Parr shaker type hydrogenation apparatus. A brass hydrogenation apparatus should not be used due to the corrosive nature of ammonia with the brass.** Melting points were determined on a Fisher-Johns melting point instrument and are uncorrected. Solutions were concentrated *in vacuo* using a rotary evaporator with a vacuum of 15-20 mbar and bath temperature of 30 °C. ¹H NMR and ¹³C NMR spectra were recorded at 400 MHz and 100 MHz, respectively. Chemical shifts were reported in parts per million (ppm, δ) using the residual solvent peaks (7.26 ppm (¹H), 77.0 ppm (¹³C), in CDCl₃) as internal standards. Low-resolution mass spectrometry (LRMS) and high-resolution mass spectrometry (HRMS) were done using electrospray ionization (ESI). Gas chromatography was performed in split-mode with a ratio of 25:1 with helium as the carrier gas. The injection port temperature was held constant at 250 °C. The GC column used was 5%-phenyl-95%-dimethylpolysiloxane; capillary 30.0 m x 0.25 mm; film thickness 0.25 μ m with a constant flow of He at 1.7 mL/min. The GC oven temperature, initially at 50 °C, was increased to 300 °C at 20 °C/min and held for 7.5 min (Program 1), or increased to 300 °C at 25 °C/min and held for 10 min (Program 2). The flame ionization detector (FID) used was held constant at 250 °C with hydrogen gas flow of 40 mL/min, air flow of 400 mL/min and the nitrogen makeup gas flow of 30 mL/min.

All *N*-alkyl-bis(cyanoethyl)amines were characterized by ¹H NMR and ¹³C NMR, low resolution mass spectrometry and melting point (where applicable) and their purities determined by elemental analysis. All *N*-alkyl-bis(aminopropyl)amines were

characterized by ^1H NMR and ^{13}C NMR, melting point (where applicable), low resolution mass spectrometry and high resolution mass spectrometry and their purities were determined by gas chromatography (FID) using two distinct temperature programs. ^1H NMR and ^{13}C NMR, mass spectra and elemental analyses were consistent with the assigned structures.

2. Experimental Section.

General Procedure for the Preparation of *N*-Alkyl-bis(cyanoethyl)amines (2-7).

Compounds **2-7** were synthesized by the bis-conjugate addition of the corresponding alkylamines to acrylonitrile in alcohol solvent at 45 °C or 70 °C until the reaction was complete as determined by TLC analysis. The synthesis of *N*-octyl-bis(cyanoethyl)amine (**2**) is representative of compounds **3-7**.

***N*-Octyl-bis(cyanoethyl)amine (2).** To acrylonitrile (13.9 mL, 212 mmol) in methanol (10 mL) at 0 °C was added octylamine (10 mL, 60.6 mmol) in methanol (14 mL) dropwise over 30 min. The ice bath was removed, the solution warmed to 45 °C and stirred for 16 h. The solvent and excess acrylonitrile were removed *in vacuo* to afford the title compound **2** (38.2 g, 98% yield) as a yellow oil: ^1H NMR (CDCl_3) δ 2.84-2.80 (m, 4H), 2.48 (t, $J = 7.3$ Hz, 2H), 2.45-2.42 (m, 4H), 1.41 (br m, 2H), 1.3-1.19 (m, 10H), 0.85 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{26}\text{N}_3$ $[\text{M} + \text{H}]^+$ 236.2. Found 236.2; m/z Calcd for $\text{C}_{16}\text{H}_{29}\text{N}_4$ $[\text{M} + \text{H} + \text{CH}_3\text{CN}]^+$ 277.2. Found 277.2; m/z Calcd for $\text{C}_{28}\text{H}_{51}\text{N}_6$ $[\text{M} + \text{H} + \text{M}]^+$ 471.4. Found 471.4; m/z Calcd for $\text{C}_{28}\text{H}_{50}\text{N}_6\text{Na}$ $[\text{M} + \text{Na} + \text{M}]^+$ 493.4. Found 493.4; GC (FID) >99% ($t_R = 10.2$ min, Program 1); Anal. Calcd for $\text{C}_{14}\text{H}_{25}\text{N}_3$: C, 71.44; H, 10.71; N, 17.85; Found: C, 71.48; H, 10.80; N, 18.03.

***N*-Decyl-bis(cyanoethyl)amine (3).** Conjugate addition of decylamine (25 mL, 126.2

mmol) in methanol (50 mL) to acrylonitrile (25 mL, 381.1 mmol) in methanol (30 mL) at 45 °C for 24 h according to the procedure for **2** afforded the title compound **3** (32 g, 96% yield) as a light yellow oil: ¹H NMR (CDCl₃) δ 2.80-2.77 (m, 4H), 2.45 (t, *J* = 7.3 Hz, 2H), 2.42-2.39 (m, 4H), 1.38 (br m, 2H), 1.27-1.17 (m, 14H), 0.82 (t, *J* = 6.6 Hz, 3H); LRMS (ESI) *m/z* Calcd for C₁₆H₃₀N₃ [M + H]⁺ 264.2. Found 264.2; *m/z* Calcd for C₁₆H₂₉N₃Na [M + Na]⁺ 286.2. Found 286.3; *m/z* Calcd for C₃₂H₅₉N₆ [M + H + M]⁺ 527.5. Found 527.5; *m/z* Calcd for C₃₂H₅₈N₆Na [M + Na + M]⁺ 549.5. Found 549.5; GC (FID) >99% (*t*_R = 11.13 min, Program 1); Anal. Calcd for C₁₆H₂₉N₃: C, 72.95; H, 11.10; N, 15.95; Found: C, 73.05; H, 11.26; N, 16.04.

N-Dodecyl-bis(cyanoethyl)amine (4). Conjugate addition of dodecylamine (22.6 g, 121.7 mmol) in methanol (20 mL) to acrylonitrile (28 mL, 425.8 mmol) in methanol (20 mL) at 45 °C for 16 h according to the procedure for **2** afforded the title compound **4** (34.5 g, 97% yield) as a white solid: mp 35-39 °C; ¹H NMR (CDCl₃) δ 2.76-2.73 (m, 4H), 2.42 (t, *J* = 7.3 Hz, 2H), 2.39-2.36 (m, 4H), 1.35 (br m, 2H), 1.24-1.16 (m, 18H), 0.79 (t, *J* = 6.6 Hz, 3H); LRMS (ESI) *m/z* Calcd for C₁₈H₃₄N₃ [M + H]⁺ 292.3. Found 292.3; *m/z* Calcd for C₃₆H₆₇N₃ [M + H + M]⁺ 583.5. Found 583.5; *m/z* Calcd for C₃₆H₆₆N₆Na [M + Na + M]⁺ 605.5. Found 605.5; GC (FID) >99% (*t*_R = 12.02 min, Program 1); Anal. Calcd for C₁₈H₃₃N₃: C, 74.17; H, 11.41; N, 14.42; Found: C, 74.38; H, 11.48; N, 14.58.

N-Tetradecyl-bis(cyanoethyl)amine (5). Conjugate addition of tetradecylamine (10 g, 46.9 mmol) in methanol (20 mL) to acrylonitrile (10.8 mL, 164.1 mmol) in methanol (10 mL) at 45 °C for 19 h according to the procedure for **2** afforded the title compound **5** (14.4 g, 96% yield) as a white solid: mp 46-48 °C; ¹H NMR (CDCl₃) δ 2.86-2.83 (m,

4H), 2.51 (t, $J = 7.3$ Hz, 2H), 2.47-2.44 (m, 4H), 1.43 (br m, 2H), 1.31-1.22 (m, 22H), 0.87 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $C_{20}H_{38}N_3$ $[M + H]^+$ 320.3. Found 320.3; m/z Calcd for $C_{20}H_{37}N_3Na$ $[M + Na]^+$ 342.3. Found 342.2; m/z Calcd for $C_{20}H_{37}KN_3$ $[M + K]^+$ 358.3. Found 358.2; m/z Calcd for $C_{40}H_{74}N_6Na$ $[M + Na + M]^+$ 661.6. Found 661.5; GC (FID) >99% ($t_R = 12.84$ min, Program 1); Anal. Calcd for $C_{20}H_{37}N_3$: C, 75.18; H, 11.67; N, 13.15; Found: C, 75.21; H, 11.77; N, 13.23.

***N*-Hexadecyl-bis(cyanoethyl)amine (6).** Conjugate addition of hexadecylamine (10.2 g, 42.3 mmol) in methanol (40 mL) to acrylonitrile (9.7 mL, 148.1 mmol) in methanol (10 mL) at 45 °C for 16 h according to the procedure for **2** afforded the title compound **6** (14.5 g, 99% yield) as a white solid: mp 55-57 °C (Lit. 53-54 °C)¹; 1H NMR ($CDCl_3$) δ 2.87-2.84 (m, 4H), 2.51 (t, $J = 6.6$ Hz, 2H), 2.48-2.44 (m, 4H), 1.44 (br m, 2H), 1.30-1.22 (m, 26H), 0.87 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $C_{22}H_{42}N_3$ $[M + H]^+$ 348.3. Found 348.3; m/z Calcd for $C_{22}H_{41}N_3Na$ $[M + Na]^+$ 370.3. Found 370.3; m/z Calcd for $C_{22}H_{41}KN_3$ $[M + K]^+$ 386.3. Found 386.3; m/z Calcd for $C_{44}H_{83}N_6$ $[M + H + M]^+$ 695.7. Found 695.6; m/z Calcd for $C_{44}H_{82}N_6Na$ $[M + Na + M]^+$ 717.6. Found 717.6; GC (FID) >99% ($t_R = 13.78$ min, Program 1); Anal. Calcd for $C_{22}H_{41}N_3$: C, 76.02; H, 11.89; N, 12.09; Found: C, 75.92; H, 12.03; N, 12.33.

***N*-Octadecyl-bis(cyanoethyl)amine (7).** Conjugate addition of octadecylamine (12.6 g, 46.7 mmol) in 1-butanol (55 mL) to acrylonitrile (10.7 mL, 163.3 mmol) in 1-butanol (10 mL) at 70 °C for 19 h according to the procedure for **2** afforded the title compound **7** (16.9 g, 97% yield) as a white solid: mp 61-62 °C (Lit. 54-55 °C)¹; 1H NMR ($CDCl_3$) δ 2.86-2.83 (m, 4H), 2.51 (t, $J = 6.6$ Hz, 2H), 2.47-2.44 (m, 4H), 1.43 (br m, 2H), 1.31-1.22 (m, 30H), 0.87 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $C_{24}H_{46}N_3$ $[M + H]^+$ 376.4.

Found 376.4; LRMS (ESI) m/z Calcd for $C_{24}H_{45}KN_3$ $[M + K]^+$ 414.3. Found 414.3; LRMS (ESI) m/z Calcd for $C_{26}H_{48}N_4$ $[M + H + CH_3CN]^+$ 417.4. Found 417.4; LRMS (ESI) m/z Calcd for $C_{48}H_{91}N_6$ $[M + H + M]^+$ 751.7. Found 751.7; LRMS (ESI) m/z Calcd for $C_{48}H_{90}N_6Na$ $[M + Na + M]^+$ 773.7. Found 773.7; GC (FID) >99% (t_R = 15.03 min, Program 1); Anal. Calcd for $C_{24}H_{45}N_3$: C, 76.74; H, 12.07; N, 11.19; Found: C, 76.93; H, 12.26; N, 11.05.

General Procedure for the Preparation of *N*-Alkyl-bis(3-aminopropyl)amines (9-14) by Catalytic Hydrogenation. Compounds **9-14** were synthesized by the catalytic hydrogenation of the corresponding dinitriles (5 – 10 g) as a slurry or solution in 100 mL of methanolic ammonia (7N) over 2 mL of Raney nickel under 50 psi of hydrogen. The synthesis of *N*-octyl-bis(3-aminopropyl)amine (**9**) is representative of compounds **10-14**.

***N*-Octyl-bis(3-aminopropyl)amine (9).** To a 500 mL hydrogenation flask was added **2** (7 g, 29.7 mmol), methanolic ammonia (7N, 100 mL) and Raney nickel (2 mL, 3X washed with methanol). The flask was transferred to the all stainless steel Parr shaker type hydrogenation apparatus, charged with hydrogen (50 psi) and shaken (1 min). **(Caution: An all stainless steel hydrogenator is necessary for this step to avoid corrosion of the hydrogenator and possible explosion.)** The flask was evacuated under aspirator vacuum (1 min) and subsequently charged with hydrogen (50 psi, 1 min) three times and the resultant slurry/solution was shaken under hydrogen at 50 psi for 24 h. The catalyst was removed via filtration through a pad of celite (washing with methanol) and the solution was concentrated *in vacuo* to afford the title compound **9** (7.1 g, 98% yield)

as a colorless oil: ^1H NMR (CDCl_3) δ 2.72 (t, $J = 7.3$ Hz, 4H, H-3), 2.44 (t, $J = 7.3$ Hz, 4H), 2.37 (t, $J = 7.3$ Hz, 2H), 1.66 (br s, 4H), 1.58 (m, 4H), 1.4 (m, 2H), 1.35-1.20 (m, 10H), 0.87 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{34}\text{N}_3$ $[\text{M} + \text{H}]^+$ 244.3. Found 244.3; HRMS (ESI) m/z Calcd for $\text{C}_{14}\text{H}_{34}\text{N}_3$ $[\text{M} + \text{H}]^+$ 244.2753. Found 244.2754; GC (FID) >99% ($t_R = 9.46$ min, Program 1; $t_R = 7.97$ min, Program 2).

***N*-Decyl-bis(3-aminopropyl)amine (10).** **3** (10 g, 38 mmol) was hydrogenated according to the procedure for **9** to afford the title compound **10** (10.1 g, 98% yield) as a colorless oil: ^1H NMR (CDCl_3) δ 2.73 (t, $J = 6.6$ Hz, 4H), 2.45 (t, $J = 7.3$ Hz, 4H), 2.38 (t, $J = 7.3$ Hz, 2H), 1.74 (br s, 4H), 1.59 (m, 4H), 1.41 (m, 2H), 1.35-1.19 (m, 14H), 0.88 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{38}\text{N}_3$ $[\text{M} + \text{H}]^+$ 272.3. Found 272.3; HRMS (ESI) m/z Calcd for $\text{C}_{16}\text{H}_{38}\text{N}_3$ $[\text{M} + \text{H}]^+$ 272.3066. Found 272.3056; GC (FID) >99% ($t_R = 10.47$ min, Program 1; $t_R = 8.77$ min, Program 2).

***N*-Dodecyl-bis(3-aminopropyl)amine (11).** **4** (5 g, 17.2 mmol) was hydrogenated according to the procedure for **9** to afford the title compound **11** (5.1 g, 98% yield) as a pale yellow oil. The analytical details were identical to those provided in the Experimental Section of the paper.

***N*-Tetradecyl-bis(3-aminopropyl)amine (12).** **5** (5 g, 15.7 mmol) was hydrogenated according to the procedure for **9** to afford the title compound **12** (5 g, 98% yield) as a yellow oil: ^1H NMR (CDCl_3) δ 2.57 (t, $J = 7.3$ Hz, 4H), 2.3 (t, $J = 7.3$ Hz, 4H), 2.23 (t, $J = 7.3$ Hz, 2H), 1.6 (br s, 4H), 1.44 (m, 4H), 1.27 (m, 2H), 1.15-1.08 (m, 22H), 0.73 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $\text{C}_{20}\text{H}_{46}\text{N}_3$ $[\text{M} + \text{H}]^+$ 328.4. Found 328.4; HRMS (ESI) m/z Calcd for $\text{C}_{20}\text{H}_{46}\text{N}_3$ $[\text{M} + \text{H}]^+$ 328.3672. Found 328.3692; GC (FID) >99% ($t_R = 12.2$ min, Program 1; $t_R = 10.15$ min, Program 2).

N-Hexadecyl-bis(3-aminopropyl)amine (13). **6** (5 g, 14.4 mmol) was hydrogenated according to the procedure for **9** to afford the title compound **13** (5.1 g, 99% yield) as a pale yellow oil: ^1H NMR (CDCl_3) δ 2.72 (t, $J = 7.3$ Hz, 4H), 2.44 (t, $J = 7.3$ Hz, 4H), 2.37 (t, $J = 7.3$ Hz, 2H), 1.92 (br s, 4H), 1.58 (m, 4H), 1.42 (m, 2H), 1.29-1.21 (m, 26H), 0.88 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $\text{C}_{22}\text{H}_{50}\text{N}_3$ $[\text{M} + \text{H}]^+$ 356.4. Found 356.4; HRMS (ESI) m/z Calcd for $\text{C}_{22}\text{H}_{50}\text{N}_3$ $[\text{M} + \text{H}]^+$ 356.3994. Found 356.4005; GC (FID) >99% ($t_R = 12.18$ min, Program 1; $t_R = 10.89$ min, Program 2).

N-Octadecyl-bis(3-aminopropyl)amine (14). **7** (5 g, 14.4 mmol) was hydrogenated according to the procedure for **9** to afford the title compound **14** (5 g, 98% yield) as a white solid: mp 82-83 °C (Lit. 81-82 °C)¹; ^1H NMR (CDCl_3) δ 2.67 (t, $J = 7.3$ Hz, 4H), 2.4 (t, $J = 7.3$ Hz, 4H), 2.33 (t, $J = 7.3$ Hz, 2H), 1.95 (br s, 4H), 1.54 (m, 4H), 1.37 (m, 2H), 1.29-1.21 (m, 30H), 0.83 (t, $J = 6.6$ Hz, 3H); LRMS (ESI) m/z Calcd for $\text{C}_{24}\text{H}_{51}\text{N}_2$ $[\text{M} - \text{NH}_2]^+$ 367.4. Found 367.4; LRMS (ESI) m/z Calcd for $\text{C}_{24}\text{H}_{54}\text{N}_3$ $[\text{M} + \text{H}]^+$ 384.4. Found 384.4; HRMS (ESI) m/z Calcd for $\text{C}_{24}\text{H}_{54}\text{N}_3$ $[\text{M} + \text{H}]^+$ 384.4285. Found 384.4318; GC (FID) >99% ($t_R = 13.99$ min, Program 1; $t_R = 12.33$ min, Program 2).

3. ¹³C NMR Data.

Supplemental Table 1. ¹³C Data for *N*-Alkyl-bis(cyanoethyl)amines.

Compound	Chemical Shift (ppm)						
	C3	C1'	C1	C2'-(CX'-2)	CX'-1	C2	CX'
(1) n = 3	118.6	53.4	49.6	31.6 - 26.7	22.5	16.9	13.9
(2) n = 5	118.6	53.3	49.4	31.6 - 27.0	22.5	16.8	13.9
(3) n = 7	118.6	53.2	49.3	31.6 - 26.9	22.4	16.6	13.9
(4) n = 9	118.6	53.1	49.1	31.5 - 26.7	22.3	16.5	13.7
(5) n = 11	118.6	53.4	49.6	31.9 - 27.1	22.6	16.9	14.1
(6) n = 13	118.6	53.5	49.7	31.9 - 27.1	22.7	17.0	14.1
(7) n = 15	118.6	53.4	49.6	31.8 - 27.0	22.6	16.9	14.1

Supplemental Table 2. ^{13}C Data for *N*-Alkyl-bis(3-aminopropyl)amines.

Compound	Chemical Shift (ppm)					
	C1'	C1	C3	C2'-(CX'-2)	CX'-1	CX'
(8) n = 3	54.1	51.9	40.8	31.8 – 26.9	22.7	14.1
(9) n = 5	54.1	51.9	40.8	31.8 – 26.9	22.6	14.1
(10) n = 7	54.1	51.9	40.8	31.9 – 26.9	22.7	14.1
(11) n = 9	54.1	51.9	40.8	31.9 – 26.9	22.6	14.1
(12) n = 11	53.9	51.6	40.4	31.6 – 26.7	22.4	13.8
(13) n = 13	54.2	51.9	40.8	31.9 – 27.0	22.6	14.1
(14) n = 15	54.1	51.8	40.7	31.8 – 26.9	22.6	14.0

4. ^1H NMR Spectra for Compounds 8-14.

5. References.

- (1) Carter, A.; Morton, D. W.; Kiely, D. E. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, 38, 3892-3899.