Efficient Synthesis of Diastereomerically Pure Vicinal Diamines: *meso*-2,3-Bis(methylamino)butane and *cis*-1,2-Bis(methylamino)cycloalkanes

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Received October 21, 1996

Vicinal diamines are excellent ligands for metal ions (Li^+, Mg^{2+}, Zn^{2+}) as well as for a multitude of pharmacological applications.[1,2] For example, their Pt(II) complexes are effective in cancer therapy. Vicinal diamines, particularly *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), are well-known catalysts for the reactions of organolithium compounds, an effect that has not been adequately explained.[3] From low-temperature NMR data, it is known that organolithium compounds form bridged dimers in the presence of TMEDA with each Li bidentately complexed to the diamine.[4] In principle, such complexes should be favored if the amino groups were constrained cis, such as in cyclic, cis vicinal tertiary diamines.

Cis vicinal analogs of TMEDA have not been investigated as potential catalysts of organolithium reactions, largely because such compounds were not commercially available. Among the many published syntheses,[5−8] few are inexpensive and efficient to carry out.[9]

Our approach is based on the reported condensation of α-hydroxy ketones or 1,2-disiloxyalkenes with ureas to give imidazolin-2-ones.[10] Then, hydrogenation of the latter followed by hydrolysis of the resulting imidazolidin-2-ones should yield a variety of vicinal (including cis vicinal) diamines. This report describes such a procedure, see Scheme 1. Thus the acid-catalyzed (0.1 equiv of tosyl acid) condensation of *N*,*N*′-dimethylurea with 3-hydroxybutanone to form 38% of 1,3,4,5-tetramethylimidazolin-2-one (**1**) is complete within 12 h in refluxing cumene.[12] At lower temperatures, using refluxing benzene or toluene only starting material was recovered from the reaction mixture. Use of reactant concentrations above 0.1 M significantly reduced the yield of **1**, most likely due to competing polymerization of the reactants.

Compound **1** was hydrogenated over PtO_2 at 1500 psi in glacial acetic acid over the course of 7 days to yield 60% of *cis*-1,3,4,5-tetramethylimidazolidin-2-one (**2**). Due to their heteroaromatic character, catalytic hydrogenation of imidazolin-2-ones is reported to be very slow and requires active catalysts as well as high pressure. Dushinsky and Dolan reported the successful use of PtO_2 as catalyst and later demonstrated that the *N*,*N*′-diacylimidazolin-2-ones underwent hydrogenation over palladium on carbon under milder conditions. Simon[13] used excess Raney nickel catalyst, but gave no details concerning yields or stereochemistry.

Through the course of our investigation, we found that **1** was inert to hydrogenation over palladium on carbon or Raney nickel (W-2). Furthermore, heating the reaction solution to 80 °C did not significantly increase the yield of **2** or substantially decrease the reaction time. Thus, this procedure should be applied to compounds which do not have functionalities which are sensitive to active hydrogenation conditions.

Compound **2** was then hydrolyzed by refluxing in 6 M aqueous HCl for 7 days to yield 83% of *meso*-2,3-bis(methylamino)butane dihydrochloride salt (**3**). Imidazolidin-2-ones are remarkably resistant to hydrolysis under a variety of acidic and basic conditions and display reactivity very similar to tetraalkylated ureas.[14] Finally, reaction of 40% NaOH regenerated the free vicinal diamine, **4**, in 94% isolated yield. This is the first synthesis of diastereomericaly pure *meso*-2,3-bis(methylamino)butane.

An attractive extension of the above procedure was to apply it to the preparation of cis, cyclic, vicinal diamines (see Scheme 2). We were unable to confirm Ruhlmann's claim that urea condenses with cyclic acyloin products in refluxing cyclohexanol/aqueous HCl to yield imidazolin-2-ones.[15] However, several cyclic acylion products condensed reproducibly with *N*,*N*′-dimethylurea in refluxing cumene containing a catalytic amount of toluenesulfonic acid. Subsequent steps used to prepare **5** through **9** with $n = 1-4$ were identical to the procedure mentioned above. The isolated yields of these compounds are listed in Table 1. As might be expected, the bicyclic imidazolidin-2-ones **7**, $n = 1-4$, are very unreactive to hydrolysis. They failed to react with hydrazine, refluxing sulfuric acid, and $Ba(OH)_2$ at 120 °C but did undergo hydrolysis in refluxing 6 M aqueous HCl.

In sum we have developed an efficient synthesis of diastereomerically pure, vicinal diamines employing inexpensive and readily available starting materials.[16] The procedure cannot be applied to molecules which have unprotected functionalities sensitive to acid or catalytic hydrogenation conditions. However, this synthesis is very useful for the preparation of the title compounds and provides a route to a class of cis vicinal diamines which have previously been difficult to prepare. We are currently investigating reactions which might further enhance the above procedure, as well as the influence of cis-tertiary-vicinal diamines prepared via the above procedure on organolithium structure and reactivity.

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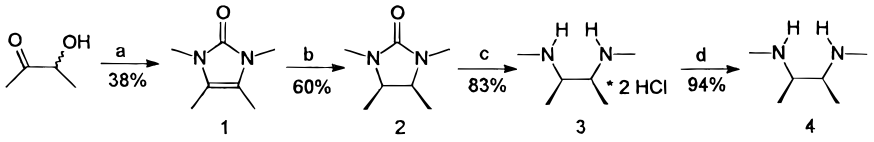
(16) All assigned structures for compounds are consistent with their spectroscopic data and method of preparation. No evidence was detected for the trans-substituted imidazolidin-2-ones.

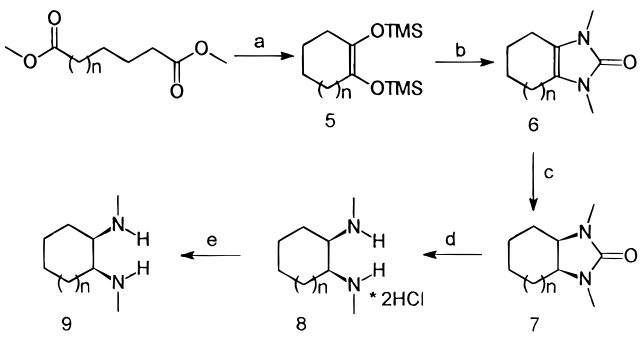
S0022-3263(96)01972-X CCC: $14.00

Scheme 1[a]



[a] Key: (a) 1,3-dimethylurea, TosOH (cat), cumene, 152 °C; (b) 1500 psi H_2, PtO_2, acetic acid, 7 days, rt; (c) 12 M HCl, 7 days, 105 °C; (d) 40% NaOH(aq).

Scheme 2[a]



[a] Key: (a) TMSCl, Na, toluene, 111 °C; (b) 1,3-dimethylurea, TosOH (cat), cumene, 152 °C; (c) 1500 psi H_2, PtO_2, acetic acid, 7 days, rt; (d) 12 M HCl, 14 days, 105 °C; (e) 40% NaOH(aq).

Table 1. Isolated Yields (%) of *cis*-1,2-Bis(methylamino)cycloalkanes

n	**5**	**6**	**7**	**8**	**9**[a]
1	58	58	76	40	95
2	79	56	74	45	92
3	45	67	62	83	96
4	46	77	78	80	92

[a] Determined by GC.

Experimental Section

All solvents, reagents, and starting materials are commercially available. FT-NMR spectra of synthetic compounds were obtained using a Bruker AC-200 spectrometer. All hydrogenations were carried out using a 450 mL Parr stainless steel bomb (model 4562) with a maxium pressure rating of 2000 psi. Platinum oxide (Adam's catalyst) was always activated by hydrogenation before use.

1,3,4,5-Tetramethylimidazolin-2-one (1). A Dean−Stark trap was attached to a round bottom flask, and a Friedrich condenser was attached to the trap. A septum was placed over the mouth of the condenser, and the system was flame dried under vacuum and purged with argon twice. Cumene (1000 mL, freshly distilled, degassed with argon) was charged into the flask together with a stir bar, followed by 1,3-dimethylurea (8.81 g, 0.100 mol), 3-hydroxybutanone (8.81 g, 0.100 mol), and *p*-toluenesulfonic acid monohydrate (1.97 g, 0.010 mol, 0.1 equiv). Since these reagents are hygroscopic they were dried in a desiccator before use to avoid misleading water measurements. The trap was filled with cumene, and a heating mantle and stirrer were attached to the flask. The reaction solution was stirred and refluxed (152 °C) for 12 h under argon. By the time *ca.* 4 mL (theoretical, 3.6 mL) of water had collected in the trap, the reaction was assumed to be complete. The solvent was removed by distillation into the open trap. The *ca.* 20 mL of a dark red oil which remained in the reaction flask was vacuum-distilled at 125 °C/3 Torr, giving a light yellow oil which solidified on standing at room temperature. To prevent product solidification in the head, the latter was warmed gently with a flame. The solid was vacuum filtered and washed with 3 mL of cold distilled water and then with 3 mL of cold acetone to yield **1** (5.32 g, 0.038 mol, 38%) as a white solid, mp 95 °C. This reaction produced lower yields when run at concentrations higher than 0.1 M. **1:** ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.75 (s, 6H), 1.58 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 153.3, 112.9, 27.1, 8.4; GC/MS/IR purity > 97%; *m*/*z* 140, calcd 140.19.

***cis*-1,3,4,5-Tetramethylimidazolidin-2-one (2).** Compound **1** (10.09 g, 0.072 mol), platinum oxide (1.00 g, 0.004 mol, 0.055 equiv), and glacial acetic acid (170 mL, freshly distilled) were charged into a Parr high-pressure hydrogenator. The chamber was closed, evacuated and purged with hydrogen three times and then pressurized to 1500 psi and stirred at room temperature for 7 days. The system was periodically checked and returned to 1500 psi as the reactants absorbed hydrogen. After 7 days, the chamber was opened and charged with Celite to destroy any unreacted catalyst. The reaction solution was filtered through a 2 cm layer of Celite on a glass frit to yield a light yellow solution which distilled to yield **2** (6.11 g, 0.043 mol, 60%) at 93 °C/3 Torr. Roughly 30% of starting material was recovered, and analysis of the product showed only the cis stereoisomer; 10% palladium on carbon was ineffective as a hydrogenation catalyst. **2:** ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.35 (m, 2H), 2.59 (s, 6H), 0.95 (d, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 161.3, 54.8, 28.5, 12.1; GC/MS/IR purity > 97%; *m*/*z* 142, calcd 142.21.

***meso*-2,3-Bis(methylamino)butane Dihydrochloride (3).** Compound **2** (6.11 g, 0.043 mol) and 12 M hydrochloric acid (108 mL, 1.296 mol, 30 equiv) was charged into a round bottom flask. A stir bar and heating mantle were added; then a Liebig condenser was attached to the flask. The solution was stirred and refluxed (105 °C) for 7 days and then rotary evaporated to dryness to yield **3** (6.75 g, 0.036 mol, 83%): mp 233 °C; ^{1}H NMR (D_2O, 200 MHz) δ 3.51 (m, 2H), 2.63 (s, 6H), 1.30 (d, 6H); ^{13}C NMR (D_2O, 50 MHz) δ 56.7, 31.3, 11.6.

***meso*-2,3-Bis(methylamino)butane (4).** Upon dissolving **3** (6.75 g, 0.036 mol) in 10 mL of 40% aqueous NaOH, a light yellow layer oiled out of solution. The basic aqueous layer was transferred to a 60 mL separatory funnel and extracted with 3 × 10 mL of diethyl ether; the organic extracts were combined, washed with 3 mL of saturated NaCl, and then dried over Na_2SO_4. The organic solution was distilled to yield **4** (4.00 g, 0.034 mol, 94%): bp = 135 °C/1 atm; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.45 (m, 2H), 2.29 (m, 6H), 1.78 (m, 2H), 0.90 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 57.9, 34.4, 15.1; GC/MS/IR purity > 97%; M^+ 116 amu, calcd 116.21 amu.

1,2-Bis(trimethylsiloxy)cyclohexene (5, *n* = 1). A three-neck, round bottom flask was fitted with a Friedrich condenser, a Herschberg stirrer, and a pressurized addition funnel. Septa were placed over the mouths of the condenser and funnel. The system was flame dried under vacuum and purged with argon twice. Toluene (700 mL, distilled from CaH_2, degassed with Ar) was charged into the flask through the addition funnel followed by sodium (27.1 g, 1.18 mol, 4.7 equiv) in pieces, cut under pentane. The solution was refluxed (110 °C) and stirred for 2 h to produce a sodium dispersion. The pressurized addition funnel was charged with toluene (250 mL), dimethyl adipate (43.55 g, 0.250 mol, distilled), and trimethylsilyl chloride (108.64 g, 1.00 mol, 4 equiv, distilled from CaH_2). The solution in the addition funnel was mixed via Ar ebulition and then added dropwise over 6 h to the refluxing reaction mixture, with stirring. The reaction mixture turned purple upon addition and then became brown one-third of the way through the addition. After addition, stirring and reflux were continued for 12 h. After being cooled to room temperature, the mixture was vacuum filtered through glass wool and then vacuum filtered through 1 cm of Celite on a glass frit to remove residual sodium particles. The resulting light yellow filtrate was distilled to yield **5** (*n* = 1) (37.19 g, 0.144 mol, 58%): bp 76−81 °C/0.4 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.04 (m, 4H), 1.57 (m, 4H), 0.15 (s, 18H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 132.1, 29.6, 23.3, 0.8.

1,2-Bis(trimethylsiloxy)cycloheptene (5, *n* = 2). The procedure described above was followed using diethyl pimelate

(58.2 g, 0.27 mol), sodium (29.3 g, 1.28 mol), and trimethylchlorosilane (135.5 g, 1.25 mol) to yield **5**, $n = 2$ (57.8 g, 0.212 mol, 79%) 86−92 °C/0.65 Torr: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.14 (t, 4H), 1.57 (m, 6H), 0.13 (s, 18H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 136.5, 33.0, 30.5, 25.5, 0.6.

1,2-Bis(trimethylsiloxy)cyclooctene (5, *n* = 3). Following the procedure described above, diethyl suberate (51.5 g, 0.224 mol), sodium (24.4 g, 1.07 mol), and trimethylchlorosilane (134.3 g, 1.24 mol) were used to yield **5**, $n = 3$ (28.4 g, 0.099 mol, 45%) 82−87 °C/0.3 Torr: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.09, 1.49, 0.13; ^{13}C NMR ($CDCl_3$, 50 MHz) δ 133.1, 31.1, 28.7, 26.4, 1.0.

1,2-Bis(trimethylsiloxy)cyclononene (5, *n* = 4). Following the above procedure, diethyl azelate (61.0 g, 0.23 mol), sodium (27.6 g, 1.2 mol), and trimethylchlorosilane (125.5 g, 1.15 mol) were used to yield **5**, $n = 4$ (32.1 g, 0.107 mol, 46%): bp 92−93 °C/0.1 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.17, 1.51, 0.17; ^{13}C NMR ($CDCl_3$, 50 MHz) δ 134.0, 30.5, 25.8, 24.9, 24.7, 1.1.

1,3-Dimethyl-4,5-tetramethyleneimidazolin-2-one (6, *n* = 1). A Dean−Stark trap was attached to a round bottom flask with a side arm. A Friedrich condenser was attached to the mouth of the trap, a septum was placed over the mouth of the condenser, and the system was flame dried under vacuum and then purged twice with argon. Cumene (700 mL, freshly distilled, degassed with Ar) was charged into the flask together with a stir bar followed by 1,3-dimethylurea (8.81 g, 0.100 mol), **5** ($n = 1$) (25.85 g, 0.100 mol) and *p*-toluenesulfonic acid monohydrate (1.97 g, 0.010 mol, 0.1 equiv). The urea and acid are hygroscopic and should be dried in a desiccator before use to avoid misleading water measurements. The trap was filled with cumene, and a heating mantle and stirrer were attached to the flask. The reaction solution was stirred and refluxed (153 °C) for 12 h under Ar. When 1.9 mL (theoretical 3.6 mL) of water had collected in the trap, the reaction was assumed to be complete. The solvent was removed by opening the valve at the bottom of the trap and allowing the condensing solvent to drain through the trap into a flask. The remaining 60 mL of a dark red oil was vacuum distilled to yield **6** ($n = 1$) (9.77 g, 0.058 mol, 58%) as a light yellow oil: bp 116−121 °C/0.07 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.90 (s, 6H), 2.09 (m, 4H), 1.57 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 153.3, 116.2, 26.7, 22.2, 19.4; GC/MS/IR purity > 95%; *m*/*z* 166, calcd 166.22.

1,3-Dimethyl-4,5-pentamethyleneimidazolin-2-one (6, *n* = 2). The procedure described above was used except **5** ($n = 2$) (54.5 g, 0.200 mol), 1,3-dimethylurea (17.6 g, 0.200 mol), and *p*-toluenesulfonic acid monohydrate (3.95 g, 0.020 mol) were used in this preparation to yield **6** ($n = 2$) (20.2 g, 0.112 mol, 56%): bp 130−137 °C/0.07 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.05 (s, 6H), 2.37 (t, 4H), 1.62 (m, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 152.9, 118.7, 29.1, 27.1, 24.3.

1,3-Dimethyl-4,5-hexamethyleneimidazolin-2-one (6, *n* = 3). Following the procedure described above **5** ($n = 3$) (22.9 g, 0.080 mol), 1,3-dimethylurea (7.04 g, 0.080 mol), and *p*-toluenesulfonic acid monohydrate (1.6 g, 0.008 mol) were used to yield **6** ($n = 3$) (10.39 g, 0.053 mol, 67%): bp 130−136 °C/0.09 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.68 (s, 6H), 2.05 (m, 4H), 1.15 (m, 4H), 0.96 (m, 4H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 153.0, 116.9, 27.8, 26.4, 25.1, 21.4.

1,3-Dimethyl-4,5-heptamethyleneimidazolin-2-one (6, *n* = 4). Following the above procedure **5** ($n = 4$) (22.2 g, 0.074 mol), 1,3-dimethylurea (6.52 g, 0.074 mol), and *p*-toluenesulfonic acid monohydrate (2.0 g, 0.010 mol) were used to yield **6** ($n = 4$) (11.99 g, 0.057 mol, 77%): bp 139−146 °C/0.08 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ, 3.06 (s, 6H), 2.40 (t, 4H), 1.6−1.2 (m, 10H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 153.6, 117.7, 26.9, 25.3, 24.5, 23.2, 20.8.

1,3-Dimethyl-4,5-tetramethyleneimidazolidin-2-one (7, *n* = 1). Compound **6** ($n = 1$) (11.47 g, 0.069 mol), platinum oxide (1.2 g, 5.27 mmol, 0.07 equiv), and glacial acetic acid (150 mL, freshly distilled) were charged into a Parr hydrogenator. The chamber was sealed, evacuated, and purged with hydrogen three times and then pressurized to 1500 psi and stirred at room temperature for 7 days. After 7 days, the chamber was opened and a scoop of Celite was added; then the reaction mixture was vacuum filtered through 1 cm of Celite on a glass frit to produce a yellow filtrate which distilled to yield **7** ($n = 1$) (8.72 g, 0.052 mol, 76%): bp 96−100 °C/0.25 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.00 (m, 2H), 2.39 (s, 6H), 1.6−0.9 (m, 8H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 162.1, 55.0, 28.2, 25.0, 20.3; GC/MS/IR purity > 95%; *m*/*z* 168, calcd 168.24.

1,3-Dimethyl-4,5-pentamethyleneimidazolidin-2-one (7, *n* = 2). Following the hydrogenation procedure described above, **6**, ($n = 2$) (18.74 g, 0.104 mol), platinum oxide (1.39 g, 6.1 mmol), and glacial acetic acid (180 mL) were used to give **7** ($n = 2$) (14.05 g, 0.077 mol, 74%): bp 104 °C/0.3 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.35 (t, 2H), 2.48 (s, 6H), 1.6−1.0 (m, 10H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.4, 59.6, 30.4, 28.4, 27.8, 24.1.

1,3-Dimethyl-4,5-hexamethyleneimidazolidin-2-one (7, *n* = 3). Following the above procedure, **6** ($n = 3$) (9.91 g, 0.051 mol), platinum oxide (0.9 g, 3.95 mmol), and glacial acetic acid (150 mL) were used to yield **7** ($n = 3$) (6.22 g, 0.032 mol, 62%): bp 117−122 °C/0.09 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.26 (t, 2H), 2.60 (s, 6H), 1.6−1.2 (m, 18H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 160.5, 61.3, 29.0, 27.3, 25.3, 23.8.

1,3-Dimethyl-4,5-heptamethyleneimidazolidin-2-one (7, *n* = 4). The above hydrogenation procedure was followed using **6** ($n = 4$) (9.37 g, 0.045 mol) and platinum oxide (1.1 g, 4.8 mmol) in glacial acetic acid (150 mL) to yield **7** ($n = 4$) (7.36 g, 0.035 mol, 78%): bp 127−129 °C/0.07 Torr; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 3.25 (t, 2H), 2.59 (s, 6H), 1.6−1.2 (m, 18H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 161.0, 62.6, 29.0, 27.7, 25.6, 25.0, 24.3.

***cis*-1,2-Bis(methylamino)cyclohexane Dihydrochloride (8, *n* = 1).** Compound **7** ($n = 1$) (8.75 g, 0.052 mol) and 12 M hydrochloric acid (130 mL, 1.56 mol, 30 equiv) were charged into a round bottom flask with a stir bar. A reflux condenser and a heating mantle were attached to the flask. The reaction mixture was refluxed (108 °C) and stirred for 2 weeks and then rotary evaporated to dryness to yield **8** ($n = 1$) (4.83 g, 0.021 mol, 40%): mp = 208 °C; ^{1}H NMR (D_2O, 200 MHz) δ 3.71 (m, 2H), 2.81 (s, 6H), 1.79 (m, 4H), 1.46 (m, 4H); ^{13}C NMR (D_2O, 50 MHz) δ 57.5, 31.4, 23.0, 20.0.

***cis*-1,2-Bis(methylamino)cycloheptane Dihydrochloride (8, *n* = 2).** Acid hydrolysis followed that above using **7** ($n = 2$) (12.7 g, 0.070 mol) and 12 M hydrochloric acid (180 mL, 2.16 mol, 30 equiv) to give **8** ($n = 2$) (7.82 g, 0.032 mol, 45%): ^{1}H NMR (D_2O, 200 MHz) δ 3.75 (m, 2H), 2.81 (s, 6H), 2.2−1.5 (m, 12H); ^{13}C NMR (D_2O, 50 MHz) δ 60.0, 31.9, 25.4, 25.3, 22.4.

***cis*-1,2-Bis(methylamino)cyclooctane Dihydrochloride (8, *n* = 3).** Following the hydrolysis procedure, described above, **7** ($n = 3$) (4.12 g, 0.021 mol) and 12 M hydrochloric acid (87 mL, 1.04 mol, 50 equiv) were used to yield **8** ($n = 3$) (4.39 g, 0.017 mol, 83%): ^{1}H NMR (D_2O, 200 MHz) δ 3.82 (t, 2H), 2.88 (s, 6H), 2.2−1.5 (m, 14H); ^{13}C NMR (D_2O, 50 MHz) δ 58.7, 32.0, 25.7, 25.0, 22.2.

***cis*-1,2-Bis(methylamino)cyclononane Dihydrochloride (8, *n* = 4).** Acid hydrolysis as above of **7** ($n = 4$) (5.05 g, 0.024 mol) with 12 M hydrochloric acid (80 mL, 0.96 mol, 40 equiv) gave **8** ($n = 4$) (5.17 g, 0.019 mol, 80%): ^{1}H NMR (D_2O, 200 MHz) δ 3.74 (t, 2H), 2.84 (s, 6H), 2.2−1.4 (m, 16H); ^{13}C NMR (D_2O, 50 MHz) δ 58.8, 32.0, 25.0, 23.3, 22.0.

***cis*-1,2-Bis(methylamino)cyclohexane (9, *n* = 1).** Compound **8** ($n = 1$) (4.83 g, 0.021 mol) was dissolved in a minimum volume of 40% aqueous NaOH. The free diamine separated as a light yellow oil, **9** ($n = 7$): 95% by GC; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.50 (m, 2H), 2.30 (s, 6H), 1.7−1.1 (m, 8H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 58.7, 34.1, 27.4, 22.3.

***cis*-1,2-Bis(methylamino)cycloheptane (9, *n* = 2).** Compound **8** ($n = 2$) (7.81 g, 0.032 mol) was dissolved in a minimum volume of 40% aqueous NaOH. Free diamine, **9**, $n = 2$, separated as a light yellow oil: 92% by GC; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.54 (t, 2H), 2.33 (s, 6H), 1.7−1.1 (m, 12H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 62.1, 34.7, 29.6, 27.8, 23.2.

***cis*-1,2-Bis(methylamino)cyclooctane (9, *n* = 3).** Compound **8** ($n = 3$) (4.39 g, 0.017 mol) was dissolved in a minimum volume of 40% aqueous NaOH to give free amine **9** ($n = 3$) as a light yellow oil (96% by GC): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.55 (t, 2H), 2.29 (s, 6H), 1.8−1.1 (m, 14H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 60.3, 34.6, 28.6, 26.9, 24.4.

***cis*-1,2-Bis(methylamino)cyclononane (9, *n* = 4).** The free diamine **9** ($n = 4$) was released as a light yellow oil from its dihydrochloride **8** ($n = 4$) as above: 92.2% by GC; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.45 (t, 2H), 2.20 (s, 6H), 1.5−1.1 (m, 16H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 59.7, 34.6, 26.5, 25.7, 23.3, 22.0.

Acknowledgment. This work and procurement of the NMR equipment was generously funded by the National Science Foundation, Grant CHE9317298, The Ohio State University Office of Research, and by a gift from the American Cyanamid Company. We thank Dr. Jose Cabral and Dr. Uta Vitinuis for their help and Mr. Bruce Dressman who initiated this research.

Supporting Information Available: Spectral data for all compounds (48 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO961972L