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Reaction of 1,2-dibromoethane with primary amines: formation of *N*,*N*′-disubstituted ethylenediamines RNH–CH_2CH_2–NHR and homologous polyamines RNH–$[CH_2CH_2NR]_n$–H

Michael K. Denk,* Mike J. Krause, Debyani F. Niyogi and Nachhattarpal K. Gill

Department of Chemistry and Biochemistry, University of Guelph, 50 Stone Road, Guelph, Ontario N1G 2W1, Canada

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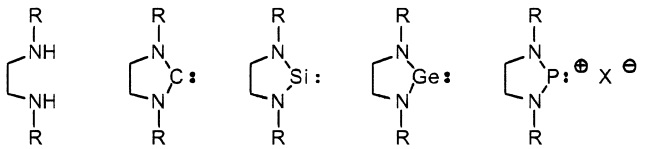
Abstract—The reaction of primary amines RNH_2 (R: Me, Et, *i*Pr, *t*Bu and Ph) with 1,2-dibromoethane gave *N*,*N*′-disubstituted ethylenediamines R–NH–CH_2CH_2–NH–R (**1**) in yields ranging from 10% (**1a**; R=Me) to 70% (**1d**, R=*t*Bu; **1e**, R=Ph). Piperazines and *N*-substituted polyethyleneimines were identified (^{1}H NMR, ^{13}C NMR and EI-MS) as side products of the reaction and isolated by fractional distillation. The piperazines **2** are formed in yields of 3–10% and can be separated from the diamines **1** in all cases, except for R=Me and Ph. The polyamine homologues RNH–$[CH_2CH_2NR]_n$–H (**3**–**5**) were isolated in yields ranging from 0.1% (*n*=4, R=*i*Pr) to 14% (*n*=2, R=*i*Pr). The yields of **1** increase with the size of the substituent R, no obvious trend exists for the yields of the side products.

1. Introduction

The *N*,*N*′-disubstituted ethylenediamines **1** and their homologous diethylenetriamines and tetramines are versatile building blocks for the synthesis of organic and inorganic compounds. They find use for the synthesis of aza-crown ethers,[1] functionalized polymers,[2] and, more recently, for the synthesis of stable carbenes,[3] stable silylenes[4] and related species[5] (Scheme 1). Their complexes with manganese,[6a] copper,[6b] and silver[6c] have been studied as homogenous catalysts and their Pd(II) and Pt(II) complexes have served as model compounds to study the interaction of *cis*-platin and related anticancer drugs with DNA.[7]



1

Scheme 1.

Despite their structural simplicity, the synthesis of *N*,*N*′-disubstituted ethylenediamines **1** and indeed of substituted ethylenediamines in general is not straightforward.[8–11] The reaction of ethylenediamine with alkylating agents like methyl iodide is known to give mixtures of polyalkylated compounds.[9,10] The introduction of *N*-protective groups[8,11] can in principle solve this problem but also adds protection and deprotection as two additional synthetic steps.[9a,11]

The reductive alkylation of ethylenediamines with acetone has been used by Gelbhard for the synthesis of the *N*-isopropyl derivatives.[9c] However, this approach only allows the introduction of substituents of the general type $RR'CH$– which excludes common substituents R such as *t*Bu or phenyl. Aldehydes form rather reduction resistant cyclic imidazolidines and are not well suited for the reductive alkylation of ethylenediamines. Acylation and subsequent reduction of the *N*-acyl amines circumvents the problem of polyalkylation but requires the use complex hydrides in stoichiometric quantities.

A potentially general route for the synthesis of *N*,*N*′-disubstituted ethylenediamines **1** that does not require multiple steps, special equipment or expensive reagents is the reaction of primary amines with 1,2-dibromoethane.

Despite earlier reports in the literature[8,12] the synthetic scope of the reaction has remained unclear. We have previously obtained *N*,*N*′-di-*tert*-butylethylenediamine and *N*,*N*′-diisopropyl ethylenediamine from the respective primary amines and 1,2-dibromoethane in the context of our research on stable carbenes,[3] silylenes,[4] and related species[5] and became interested to see if the developed methodology could be extended to other primary amines as well.

Keywords: amines; polyethyleneimine; alkylation; chelate ligands; ethylenediamine.
* Corresponding author. Tel.: +1-5198244120x53820; fax: +1-5197661499; e-mail: mdenk@uoguelph.ca

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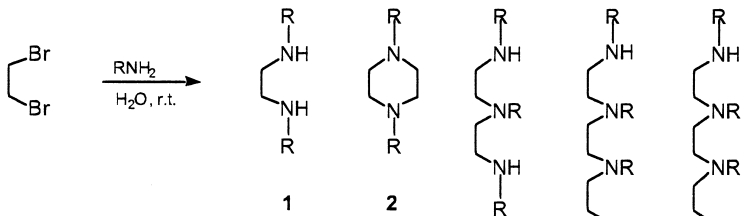

R	1	2	3	4	5
Me (a)	10%	9%	2%	1%	—
Et (b)	28%	3%	6%	2%	—
i-Pr (c)	49%	7%	14%	1%	0.1%
t-Bu (d)	70%	9%	2%	—	—
Ph (e)	70%	10%	10%	—	—

Scheme 2.

2. Results

The reactions of 1,2-dibromoethane with primary amines RNH_2 were carried out at room temperature with a set of identical reaction conditions (see below) for R=Me, Et, *i*Pr and *t*Bu. Aniline, which was included as a representative of aromatic amines, was found to be less reactive and required heating.

GC-MS analysis of the crude amine mixtures showed the formation of the desired substituted ethylenediamines **1** but also demonstrated the formation of the piperazines **2** and polyamines **3**–**5** as volatile side products (Scheme 2)[18] which were isolated by fractional distillation and characterized by spectroscopic methods (^{1}H, ^{13}C and GC-MS).

The best yields of **1** were obtained by reacting 1,2-dibromoethane (1 equiv.) with an excess of the primary amine (5 equiv.). Attempts to use the addition of auxiliary bases like NaOH or Na_2CO_3 to reduce the amount of primary amine to the theoretically required amount (2 equiv.) led to lower yields. The yield of the diamines **1** increased in a regular fashion with the steric bulk of the substituent from R=Me to R=*t*Bu; no obvious correlation existed for the yields of **2**–**5**.

The reactions did not require organic solvents but an adequate amount of water greatly facilitated stirring by keeping the voluminous amine hydrobromide salts which form in the course of the reaction dissolved. Methylamine and ethylamine were accordingly used in form of the readily available aqueous solutions. Apart from facilitating stirring, the presence of water also accelerates the reactions.[13] This effect was first noticed for *tert*-butyl amine which gave a 75–80% yield of **1d** after only 24 h at room temperature in water as solvent whereas, the reaction in hexanes (no water) required 4 days of boiling and the use of an efficient overhead stirrer to give **1d** in 50% yield.

Unlike *tert*-butylamine, the sterically less hindered amines (R=Me, Et, *i*Pr) reacted in exothermic fashion and required ice cooling and slow mixing of the components to prevent losses of the volatile amine. Despite their initial exothermic nature, completion still required ~2 weeks at room temperature which exceeded the reaction time required for R=*t*Bu (3 days). This discrepancy may result from solubility effects operating in the generally biphasic reaction mixtures. While the lipophilic 1,2-dibromoethane will reside predominantly in the organic phase, the amines will reside in the aqueous phase for R=Me, Et and *i*Pr but in the organic phase for R=*t*Bu.

The use of water or the sequence of the addition of the reagents did not significantly influence the product distribution.

The less reactive aniline required heating which (contrast to R=alkyl) was also required to prevent a solidification of the reactions mixture. With the exception of aniline, the reactions were conveniently carried out in ordinary screw cap storage bottles connected to a bubbler and inert gas line.

Fractional distillation over a 20 cm Vigreux column separated the homologous amines **1**, **3**, **4**, and **5** (GC control) but gave mixtures of the ethylenediamines **1** and piperazines **2** that required redistillation.[14] Distillation failed to separate **1a/2a** (azeotrope) and **1e/2e** (small boiling point difference). Pure materials (GC) were obtained by counter current extraction with hexane–water which leads to enrichment of the more lipophilic piperazines **2** in the organic phase. Complete separation was also achieved by column filtration of the piperazine/ethylenediamine mixtures (ca. 1 g of mixture in 10 mL of hexanes) through a 30 cm column of neutral Al_2O_3. The piperazines have significantly lower retention times and are thus readily separated from the diamines which were obtained as second fraction with the more polar CH_2Cl_2 as eluent. The former method is better suited for large quantities while the column filtration is better suited for small amounts.

The generally very hygroscopic alkyl substituted ethylenediamines required extensive drying over solid NaOH and subsequent distillation over sodium. Distillation over NaOH or CaH_2 was found to be insufficient.

The multiplicities and relative intensities of the ^{1}H and ^{13}C

signals and the comparison of the shifts in **2**–**5** with those of **1** allowed the assignment of most signals, although the assignment becomes more difficult with increasing chain length. The terminal methylene protons RNHCH_2 were observed as broad singlets, triplets or with higher multiplicities (e.g. q). H,D-exchange experiments with D_2O reduced the signals to triplets and confirmed that the higher multiplicities were caused by coupling with the NH protons.

The EI-MS spectra of the ethylenediamines (**1**, **3**–**5**) showed [M+1] peaks[15] which presumably result from the formation of stable hydrates (and loss of [OH]$^-$) in the spectrometer. The less hygroscopic piperazines show the usual $[M]^{+\cdot}$ peaks.

3. Experimental

Melting points were recorded in sealed capillaries and are uncorrected. GC-MS spectra were obtained with a Varian CP-3800 GC/Saturn 2000 MS combination at an ionizing voltage of 70 eV and a 30 m×0.25 mm Varian CP 5860 low bleed phenyl-dimethylsiloxane column (5% phenyl). Temperature program: 4 min at 50°C; 10 min constant heating rate of 20°C/min; 6 min at 250°C. NMR-spectra (chemical shifts in δ) were recorded with a Bruker 400 MHz spectrometer at normal spectrometer temperature. The NMR spectra are referenced versus TMS (^{1}H and ^{13}C, internal) and were obtained with flame sealed samples. All starting materials were obtained from Aldrich Inc. and used as received. The products were handled in an atmosphere of nitrogen or argon (purity 99.994 or better). Yields refer to isolated products unless noted otherwise and are not optimized. HR-MS data of the previously unknown amines (**4c**, **5c**) were obtained with a VG ZAB-R instrument at the McMaster Regional Centre for Mass Spectrometry, Hamilton, Ontario. All previously described compounds are identified by their CAS numbers (in square brackets, see below).

3.1. General procedure for the reaction of primary amines with 1,2-dibromoethane

The primary amine (5 mol), water (300 mL) and 1,2-dibromoethane (1 mol, 86 mL) were mixed in a bottle of suitable size and magnetically stirred at room temperature for 2 weeks. Initial ice cooling was required for the sterically less hindered alkyl amines (R=Me, Et and *i*Pr). Aniline was reacted by boiling for 24 h in a round bottom flask equipped with a magnetic stirrer and reflux condenser. The free amines are obtained by adding NaOH pellets in 20 g portions under ice cooling and constant stirring until the NaOH remains undissolved (caution: gas evolution for methylamine and ethylamine). The crude amine layer (top) was separated, stirred with 50 g of NaOH pellets for 24 h and decanted. The procedure was repeated until the NaOH remained undissolved. The amines **1**–**5** were isolated by fractional distillation of the crude, predried (NaOH) amine mixture over 5 g of sodium with the help of a 30-cm Vigreux column. For isolated yields, see Scheme 2.

The incompletely separated fractions containing **1a/2a** and **1e/2e** were dissolved in a tenfold volume of hexanes and filtered through a 30 cm column of neutral Al_2O_3 (10 g/1 g of amine mixture). The filtrates were collected in 5 mL fractions and the pure (by GC) fractions combined, to give, after evaporation of the solvent in vacuo, the pure amines **1a**, **2a**, **1e** and **2e**. Recovery >90%.

3.1.1. *N*,*N*′-Dimethylethylenediamine (1a). CAS [110-70-3]. Colorless oil, bp 121–123°C (azeotrope with **2a**), bp 119–120°C (pure), lit.[11a] 120°C. ^{1}H (C_6D_6): 1.03 [s, br, 2H, N*H*], 2.33 [s, 6H, NCH_3], 2.55 [s, 4H, NCH_2]. ^{13}C (C_6D_6): 36.7 [N*C*H$_3$], 52.0 [N*C*H$_2$]. GC-MS: t_r=3.25 min, *m*/*z* (rel. int. %)=101(20), 89(75), 75(5), 71(3), 58(100), 57(50), 56(25).

3.1.2. 1,4-Dimethylpiperazine (2a). CAS [106-58-1] Colorless oil, bp 127–130°C, lit.[17] 130°C. ^{1}H (C_6D_6): 2.13 [s, 6H, NCH_3], 2.33 [s, 8H, NCH_2], ^{13}C (C_6D_6): 46.2 [NCH_3], 55.5 [N*C*H$_2$]. GC-MS: t_r=4.98 min, *m*/*z* (rel. int. %)=144(100), 99(10), 85(15), 71(30), 70(35), 58(25), 57(20), 56(30).

3.1.3. 1,4,7-Trimethyl-1,4,7-triazaheptane (3a). CAS [105-84-0]. Colorless oil, bp 55–56°C/0.1 Torr, lit.[6a] 60°C/1 Torr. ^{1}H (C_6D_6): 1.05 [s, 2H, N*H*], 2.10 [s, 3H, 4-CH_3], 2.32 [s, 6H, 1,7-CH_3], 2.36 [t, 4H, ^3J(H,H)=6 Hz, HNCH$_2$CH_2], 2.53 [t, 4H, ^3J(H,H)=6 Hz, HNCH_2CH$_2$]. ^{13}C (C_6D_6): 36.8 [HN*C*H$_3$], 42.4 [C$_2$N*C*H$_3$], 50.1 [HN*C*H$_2$], 57.8 [HNCH$_2$*C*H$_2$]. GC-MS: t_r=8.24 min, *m*/*z* (rel. int. %)=146(20), 114(5), 101(35), 89(5), 72(15), 58(100).

3.1.4. 1,4,7,10-Tetramethyl-1,4,7,10-tetraazadecane (4a). CAS [105-78-2]. Colorless, viscous oil, bp 89–90°C/0.1 Torr, lit.[6a] 92°C/1 Torr. ^{1}H (C_6D_6): 1.24 [s, 2H, N*H*], 2.12 [s, 6H, C$_2$NCH_3], 2.13 [s, 6H, NHCH_3], 2.39 [s, 5,6-CH_2], 2.40 [t, 4H, ^3J(H,H)=7 Hz, NHCH$_2$CH_2], 2.55 [q, 4H, ^3J(H,H)=7 Hz, NHCH_2CH$_2$]. ^{13}C (C_6D_6) 36.8 [4,7-*C*H$_3$], 42.8 [1,10-*C*H$_3$], 50.2 [5,6-*C*H$_2$], 56.4 [2,9-*C*H$_2$], 57.8 [NHCH$_2$*C*H$_2$]. EI-MS (direct inlet): *m*/*z* (rel. int. %)=203(100) $[M+1]^+$, 129(5), 115(7), 72(12).

3.1.5. *N*,*N*′-Diethylethylenediamine (1b). CAS [111-74-0]. Colorless oil, bp 152–153°C, lit.[11a] 151–152°C. ^{1}H (C_6D_6): 0.91 [s, 2H, N*H*], 1.01 [t, 6H, ^3J(H,H)=7 Hz, NCH$_2$CH_3], 2.53 [q, 4H, ^3J(H,H)=7 Hz, NCH_2CH$_3$], 2.60 [s, 4H, NCH_2CH_2]. ^{13}C (C_6D_6): 15.8 [N*C*H$_2$CH$_3$], 44.5 [N*C*H$_2$CH$_3$], 50.0 [N*C*H$_2$*C*H$_2$]. GC-MS: t_r=6.2 min, *m*/*z* (rel. int. %)= 117(20) $[M+1]^+$, 72(20), 58(100).

3.1.6. *N*,*N*′-Diethylpiperazine (2b). CAS [102459-01-8]. Colorless oil, bp 171–172°C, lit.[9c] 169–171°C, lit.[17]174–176°C. ^{1}H (C_6D_6): 0.99 [t, 6H, ^3J(H,H)=7 Hz, N–CH$_2$CH_3], 2.25 [q, 4H, ^3J(H,H)=7 Hz, NCH_2CH$_3$], 2.40 [s, 8H, NCH_2CH_2]. ^{13}C (C_6D_6): 12.6 [*C*H$_3$], 52.6 [N*C*H$_2$CH$_3$], 53.4 [N*C*H$_2$*C*H$_2$]. GC-MS: t_r=7.50 min, *m*/*z* (rel. int. %)=142(100), 127(30), 113(15), 99(30), 84(75), 70(75), 56(80).

3.1.7. 1,4,7-Triethyl-1,4,7-triazaheptane (3b). CAS [105-93-1]. Colorless, viscous oil, bp 66–67°C/0.1 Torr, lit.[9c] 102–105°C/11 Torr. ^{1}H (C_6D_6): 0.93 [t, 3H, ^3J(H,H)=7 Hz, C$_2$NCH$_2$CH_3], 1.06 [t, 6H, ^3J(H,H)=7 Hz, HNCH$_2$CH_2], 1.20 [s, 2H, N*H*], 2.40 [q, 2H, ^3J(H,H)=7 Hz, C$_2$NCH_2CH$_3$], 2.57 [q, 4H, ^3J(H,H)=6 Hz, NHCH_2CH$_3$], 2.47 [t, 4H, ^3J(H,H)=4 Hz, NHCH$_2$CH_2], 2.60 [t, 2H,

^3J(H,H)=6 Hz, HNCH_2CH$_2$]. ^{13}C (C_6D_6): 11.0 [4-CH$_2$CH_3], 15.0 [1,7-CH$_2$CH_3], 43.3 [HNCH$_2$CH_2], 46.9 [HNCH_2CH$_3$], 47.2 [C$_2$NCN_2CH$_3$], 52.9 [HNCH_2CH$_2$]. GC-MS: t_r=9.9 min, *m/z* (rel. int.%)=188(10) [M+1]$^+$, 129(25), 86(75), 72(100), 58(40).

3.1.8. 1,4,7,10-Tetraethyl-1,4,7.10-tetraazadecane (4b). CAS [24426-33-3]. Colorless, viscous oil, bp 139–140°C/0.1 Torr, lit.[1g] 85–86°C/0.07 Torr, lit.[9c] 75–77°C/0.2 Torr. ^{1}H (C_6D_6): 0.97 [t, 6H, ^3J(H,H)=7 Hz, 4,7-CH$_2$CH_3], 1.09 [t, 6H, ^3J(H,H)=7 Hz, NHCH$_2$CH_3], 1.35 [s, 2H, N*H*], 2.50 [s, 4H, 5,6-NCH_2], 2.43 [q, 4H, ^3J(H,H)=7 Hz, NHCH_2CH$_3$], 2.62 [q, 4H, ^3J(H,H)=7 Hz, 4,7-CH_2CH$_3$], 2.52 [t, 4H, ^3J(H,H)=6 Hz, HNCH$_2$CH_2], 2.63 [t, 4H, ^3J(H,H)=6 Hz, HNCH_2CH$_2$]. ^{13}C (C_6D_6): 12.6 [4,7-CH$_2$*C*H$_3$], 15.8 [1,10-CH$_2$*C*H$_3$], 44.7 [5,6-*C*H$_2$], 48.3 [1,10-*C*H$_2$CH$_3$], 48.8 [4,7-*C*H$_2$CH$_3$], 53.0, 54.5 [N*C*H$_2$CH$_2$]. GC-MS: t_r=11.5 min, *m/z* (rel. int. %)=259(5) [M+1]$^+$, 144(30), 129(40), 86(100), 72(90), 58(45).

3.1.9. *N*,*N*′-Diisopropylethylenediamine (1c). CAS [4013-94-9]. Colorless oil, bp 169–170°C, lit.[11a] 169–171°C. ^{1}H (C_6D_6): 0.98 [d, 12H, ^3J(H,H)=6 Hz, NHCH(C*H*3)$_2$], 0.88 [s, 2H, N*H*], 2.58 [s, 4H, NCH_2], 2.66 [sept, 2H, ^3J(H,H)=6 Hz, C*H*(CH$_3$)$_2$]. ^{13}C (C_6D_6): 23.4 [CH(*C*H$_3$)$_2$], 48.0 [*C*H(CH$_3$)$_2$], 50.7 [N*C*N$_2$]. GC-MS: t_r=7.2 min, *m/z* (rel. int. %)=145(75) [M+1]$^+$, 86(25), 72(100), 58(25).

3.1.10. 1,4-Diisopropylpiperazine (2c). [CAS 21943-18-01]. Colorless, viscous oil, bp 178–180°C, lit.[9c] 93–94°C/13 Torr. ^{1}H (C_6D_6): 0.90 [d, 12H, ^3J(H,H)=6 Hz, NCH (CH_3)$_2$], 2.46 [s, 8H, NCH_2], 2.73 [sept, 2H, ^3J(H,H)=6 Hz, NC*H*(CH$_3$)$_2$]. ^{13}C (C_6D_6): 18.7 [NCH(*C*H$_3$)$_2$], 49.0 [N*C*H$_2$], 54.4 [N*C*H (CH$_3$)$_2$]. GC-MS: t_r=9.16 min, *m/z* (rel. int. %)=170(40), 155(100), 140(5), 127(15), 112(25), 98(60), 84(75), 70(30), 56(80).

3.1.11. 1,4,7-Triisopropy1-1,4,7-triazaheptane (3c). CAS [10524-50-2]. Colorless, viscous oil, bp 79–80°C/0.1 Torr, lit.[9c] 123–125°C/14 Torr. ^{1}H (C_6D_6): 0.89 [d, 6H, ^3J(H,H)=7 Hz, 4-CH(CH_3)$_2$], 1.07 [d, 12H, ^3J(H,H)=7 Hz, 1,7-CH (CH_3)$_2$], 1.30 [s, 2H, N*H*], 2.43 [t, 4H, ^3J(H,H)=6 Hz, 3,5-CH_2], 2.57 [br, 4H, ^3J(H,H)=6 Hz, 2,6-CH_2], 2.74 [sept, 2H, ^3J(H,H)=6 Hz, 1,7-C*H*(CH$_3$)$_2$], 2.80 [sept, 1H, ^3J(H,H)=6 Hz, 4-C*H*(CH$_3$)$_2$]. ^{13}C (C_6D_6): 18.3 [4-CH (*C*H$_3$)$_2$], 23.7 [1.7-CH (*C*H$_3$)$_2$], 46.8 [3,5-NCH_2], 49.2 [1,7-*C*H (CH$_3$)$_2$], 50.3 [HNCH_2], 50.5 [4-*C*H(CH$_3$)$_2$]. GC-MS: t_r=10.8 min, *m/z* (rel. int. %)=230(80) [M+1]$^+$, 157(5), 100(100).

3.1.12. 1,4,7,10-Tetraisopropyl-1,4,7,10-tetraazadecane (4c). No CAS entry. Colorless, viscous oil, bp 160–161°C/0.1 Torr. ^{1}H (C_6D_6): 0.96 [d, 12H, ^3J(H,H)=6 Hz, 4,7-CH(CH_3)$_2$], 1.09 [d, 12H, ^3J(H,H)=6 Hz, 1,10-CH(CH_3)$_2$], 1.44 [s, 2H, N*H*], 2.47 [s, 4H, 5,6-CH_2], 2.52 [pseudo-q, 4H, ^3J(H,H)=7 Hz, 2-CH_2], 2.62 [br, 4H, 3-CH_2], 2.76 [sept, 2H, ^3J(H,H)=7 Hz, C*H*(CH$_3$)$_2$], 2.85 [sept, ^3J(H,H)=7 Hz, C*H*(CH$_3$)$_2$]. ^{13}C (C_6D_6): 18.4 [4,7-CH(*C*H$_3$)$_2$], 23.6 [1,10-CH(*C*H$_3$)$_2$], 46.8 [N*C*H$_2$], 49.3 [N*C*H$_2$], 51.1, 51.2, 51.5 [NCH_2+N*C*H (CH$_3$)$_2$]. GC-MS: t_r=13.1 min, *m/z* (rel. int. %)=315(75) [M+1]$^+$, 169(25), 100(100). EI HRMS *m/z* calcd. for C$_{18}$H$_{43}$4$_5$ [M+H]$^+$: 315.3488. Found: 315.3479.

3.1.13. 1,4,7,10,13-Pentaisopropy1-1,4,7,10,13-pentaazatridecane (5c). No CAS entry. Colorless, viscous oil, bp 184–185°C/0.1 Torr. ^{1}H (C_6D_6): 0.96 [d, 12H, ^3J(H,H)=7 Hz, 4,10-CH(CH_3)$_2$], 0.99 [d, 6H, ^3J(H,H)=6 Hz, 7-CH(CH_3)$_2$], 1.09 [d, 12H, ^3J(H,H)=6 Hz, 1,13-CH (CH_3)$_2$], 1.48 [s, N*H*], 2.53 [s, 12H, 3,5,6,8,9,11-CH_2], 2.63 [mult. 4H, 2,12-CH_2], 2.78 [sept, 2H, ^3J(H,H)=6 Hz, 1,13-C*H*(CH$_3$)$_2$], 2.87 [sept, 3H, ^3J(H,H)=7 Hz, 4,7,10-C*H*(CH$_3$)$_2$]. ^{13}C (C_6D_6): 18.3 [4,10-CH(*C*H$_3$)$_2$], 18.5 [7-CH(*C*H$_3$)$_2$], 23.4 [1,13-CH(*C*H$_3$)$_2$], 46.8, 49.2, 51.1, 51.2, 51.5, 52.0, 52.2 [NCH_2+N*C*H(CH$_3$)$_2$]. GC-MS: t_r=15.3 min, *m/z* (rel. int. %)=400(10) [M+1]$^+$, 169(100), 100(55). EI HRMS *m/z* calcd. for C$_{23}$H$_{54}$N$_5$ [M+H]$^+$: 400.4379. Found: 400.4379.

3.1.14. *N*,*N*′-Di-*tert*-butylethylenediamine (1d). CAS [4062-60-6]. Colorless, oil, bp 196–198°C lit.[11a] 196–198°C. ^{1}H (C_6D_6): 0.75 [s, 2H, N*H*], 1.04 [s, 18H, C(CH_3)$_3$], 2.57 [s, 4H, NCH_2]. ^{13}C (C_6D_6): 29.4 [C(*C*H$_3$)$_3$], 43.6 [N*C*H$_2$], 49.8 [*C*(CH$_3$)$_3$]. GC-MS: t_r=8.2 min, *m/z* (rel. int. %)=173(100) [M+1]$^+$, 157(10) [M−CH$_3$]$^+$, 100(10).

3.1.15. 1,4-Di-*tert*-butylpiperazine (2d). [CAS 10125-77-6]. Isolated as colorless solid by fractional distillation and further purified by filtration of a hexane solution (~10%) over neutral Al$_2$O$_3$, bp 205–206°C, mp 83.5–84.5°C ^{1}H (C_6D_6): 1.02 [s, 18H, C(CH_3)$_3$], 2.53 [s, 8H, NCH_2]. ^{13}C (C_6D_6): 26.1 [C(*C*H$_3$)$_3$], 46.8 [N*C*H$_2$], 53.1 [*C*(CH$_3$)$_3$]. GC-MS: t_r=10.0 min, *m/z* (rel. int. %)=198(15), 183(100), 157(5), 141(5), 127(55), 112(5), 98(10), 85(20), 70(15), 56(20).

3.1.16. 1,4,7-Tri-*tert*-butyl-1,4,7-triazaheptane (3d). CAS [24426-18-4]. Colorless, viscous oil, bp 94–95°C/0.1 Torr, lit. [9c] 148–150°C/17 Torr. ^{1}H (C_6D_6): 0.75 [s, 2H, N*H*], 1.03 [s, 9H, 4-C(*C*H$_3$)$_3$], 1.11 [s, 18H, 1,7-C(*C*H$_3$)$_3$], 2.55–2.65 [m, 8H, NCH_2]. ^{13}C (C_6D_6): 27.4 [4-C(*C*H$_3$)$_3$], 29.5 [1,7-C (*C*H$_3$)$_3$], 44.1 [NH*C*H$_2$], 49.8 [NH*C*(CH$_3$)$_3$], 52.8 [*C*H$_2$N(*t*Bu)*C*H2], 54.6 [C$_2$N*C*(CH$_3$)$_3$]. GC-MS: t_r=11.5 min, *m/z* (rel. int. %)=272(50) [M+1]$^+$, 256(5) [M−CH$_3$]$^+$, 185(60), 173(10), 157(10), 129(75), 113(10), 100(100), 73(80), 57(20).

3.1.17. *N*,*N*′-Diphenylethylenediamine (1e). CAS [150-61-8]. Colorless solid, mp 68.5–69.0°C, lit [14] 65–67°C, bp 160–162°C/0.1 Torr. ^{1}H (C_6D_6): 2.79 [s, 4H, CH_2], 3.19 [s, 2H, N*H*], 6.40 [d, 4H, ^3J(H,H)=7 Hz, *ortho*-C$_6$H$_5$], 6.76 [t, 2H, ^3J(H,H)=7 Hz, *para*-C$_6$H$_5$], 7.15 [t, 4H, ^3J(H,H)=8 Hz, *meta*-C$_6$H$_5$], ^{13}C (C_6D_6): 43.0 [*C*H$_2$], 113.2 [*ortho*-*C*$_6$H$_5$], 117.8 [*para*-C$_6$H$_5$], 129.5 [*meta*-*C*$_6$H$_5$], 148.5 [*ipso*-*C*$_6$H$_5$]. GC-MS: t_r=15.6 min, *m/z* (rel. int. %)=212(25) [M]$^{+\cdot}$, 106(100), 77(35).

3.1.18. 1,4-Diphenylpiperazine (2e). CAS [613-39-8]. Colorless solid, mp 164–165°C, lit.[16a] 164–165°C, lit.[16b] 164.3°C ^{1}H (C_6D_6): 2.94 [s, 8H, NCH_2], 6.40 [d, 4H, ^3J(H,H)=7 Hz, *ortho*-C$_6$H$_5$], 6.85 [t, 2H, ^3J(H,H)=7 Hz, *para*-C$_6$H$_5$], 7.22 [t, 4H, ^3J(H,H)=7 Hz, *meta*-C$_6$H$_5$]. ^{13}C (C_6D_6): 49.3 [*C*H$_2$], 116.7 [*ortho*-*C*$_6$H$_5$], 120.1 [*para*-*C*$_6$H$_5$]. 129.3 [*meta*-*C*$_6$H$_5$], 151.8 [*ipso*-C$_6$H$_5$]. GC-MS: t_r=15.6 min, *m/z* (rel. int. %)=238(100) [M]$^+$, 223(20), 196(15), 132(55), 105(60), 104(74), 77(50).

3.1.19. 1,4,7-Tripheny1-1,4,7-triazaheptane (3e). CAS

[68360-81-6]. Colorless solid, mp 118–119°C, bp 250–252°C/0.1 Torr. ^{1}H (C_6D_6): 2.90 [pseudo-q, 4H, ^3J(H,H)=6 Hz, NHCH_2], 3.05 [t, 4H, ^3J(H,H)=7 Hz, NHCH$_2$CH_2], 3.17 [s, 2H, N*H*], 6.36 [d, 4H, ^3J(H,H)=8 Hz, *ortho*-C_6H_5NH], 6.61 [d, 2H, ^3J(H,H)=9 Hz, *ortho*-$C_6H_5NC_2$], 6.74 [t, 2H, ^3J(H,H)=7 Hz, *para*-C_6H_5NH], 6.80 [t, 1H, ^3J(H,H)=7 Hz, *para*-$C_6H_5NC_2$], 7.14 [t, 4H, ^3J(H,H)=8 Hz, *meta*-C_6H_5NH], 7.22 [t, 2H, ^3J(H,H)=7 Hz, *meta*-$C_6H_5NC_2$]. ^{13}C (C_6D_6): 41.3 [NH*C*H$_2$], 50.9 [NHCH$_2$*C*H$_2$], 113.1 [*ortho*-C_6H_5NH], 113.3 [*ortho*-$C_6H_5NC_2$], 117.5 [*para*-$C_6H_5NC_2$], 117.8 [*para*-C_6H_5NH], 129.7 [*meta*-C_6H_5NH], 129.9 [*meta*-$C_6H_5NC_2$], 148.3 [*ipso*-C_6H_5NH], 148.4 [*ipso*-$C_6H_5NC_2$]. EI-MS (direct inlet): *m/z* (rel. int. %)=332(74) [M+1]$^+$, 225(45), 212(50), 132(28), 120(100), 106(46), 91(26), 77(48), 65924).

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10. A notable exception is the reaction of ethylenediamine with isopropyl bromide which gives only two readily separated products, *N*,*N*′-diisopropylethylenediamine (57%) and *N*,*N*,*N*′-tris-isopropylethylenediamine (8%). Denk, M. K.; Krause, M. J. Unpublished results.

11. Schneider (Ref. 4a) obtained *N*,*N*′-dimethylethylenediamine from *N*,*N*′-disulfonylethylenediamine in 15% yield. See also (a) Boon, W. R. *J. Chem. Soc.* **1947**, 307–318. (b) Braun, J. v.; Heider, K.; Müller, E. *Chem. Ber.* **1918**, *51*, 737–741. (c) Johnson, T. B.; Bailey, G. C. *J. Am. Chem. Soc.* **1916**, *38*, 2135–2145.

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13. A runaway reaction occurred upon the addition of 5 mL of water to a mixture of isopropylamine (5 mol) with 1, 2-dibromoethane (1 mol).
14. Pure **1e** (mp 68.5–69.0°C) was obtained after repeated recrystallization from isopropanol or by Al_2O_3 filtration as described in the Section 3. Commercially available *N*,*N*′-diphenylethylenediamine (Aldrich D2, 700-4N, mp 65–67°C) contains ca. 2% of *N*,*N*′-diphenylpiperazine. Previously reported melting points (a) Schönberg, A. *Chem. Ber.* **1983**, *116*, 2068–2073, (65–67°C). (b) Schönberg, A. *Chem. Ber.* **1984**, *117*, 3388–3399, (64–66°C).
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18. Quarternary ammonium salts were suggested as other possible side products by one referee. While we have no evidence for their formation under the reaction conditions employed, their formation under more forcing conditions seems indeed likely.