Condensation of Alkanediamines with Formaldehyde; Intramolecular Disproportionation of *N*-Hydroxymethyl Groups into *N*-Methyl and *N*-Formyl Groups

Johannes Dale and Turid Sigvartsen

Kjemisk institutt, Universitetet i Oslo, N-0315 Oslo 3, Norway

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The condensation of α,ω-alkanediamines $NH_2(CN_2)_nNH_2$ with aqueous formaldehyde has been studied by NMR spectroscopy of isolated products and of product mixtures. The condensation was reversible and gave products of widely different types depending on alkane chain length: bicyclic oxadiaza compounds (n = 2, 3, 4), a tricyclic tetraaza compound (n = 2), a quinquecyclic octaaza compound (n = 3), two-dimensional polymers (n = 4, 5). A slow irreversible rearrangement gave in two cases (n = 3, 4), unicyclic 1-formyl-3-methyl-1,3-diaza compounds.

The condensation of *N,N'*-dimethyl-α,ω-alkandediamines $CH_3NH(CH_2)_nNHCH_3$ with aqueous formaldehyde was also studied. The reversible formation of simple unicyclic diaza compounds was observed in all cases (n = 2, 3, 4), but in one case (n = 2) there was again a slow irreversible rearrangement to the *N*-formyl-*N,N'N'*-trimethyl derivative.

The rearrangement reaction involves a hydride shift and is strictly intramolecular. The conditions for its occurrence can be understood on a conformational basis.

The reversible formation of imines (Schiff bases) from primary amines and aldehydes (e.g. benzaldehyde) has been exploited to ensure monoalkylation by quaternization of the imine and subsequent hydrolysis.[1] It has also been claimed[2] that diprimary α,ω-alkanediamines can be selectively *N,N'*-dialkylated in good yields through the formation of the bis-imine with benzaldehyde, methylation, and hydrolysis. In our hands this reaction, when applied to 1,2-ethanediamine, gave rise to complicated product mixtures.

Since formaldehyde is known to give various multicyclic condensation products with diprimary alkanediamines,[3,4] it seemed of interest to explore the possibility of using such tertiary aminals to prepare, by double alkylation, protected quaternary intermediates, which upon hydrolysis should afford disecondary alkanediamines. The extensive work by Krässig[4] on these condensation reactions needed, however, to be re-examined by means of NMR spectroscopic methods. Thus, one of the proposed structures has already been corrected,[5,6] and other products were overlooked.[6,7] In particular, Krässig based many structural conclusions on the elemental analysis of subsequently prepared derivatives, and his conclusions must be looked upon with scepticism since these condensations are easily reversible. Traces of humidity are always present, and water must be considered as an acidic catalyst *vis-à-vis* these basic and reactive aminals.

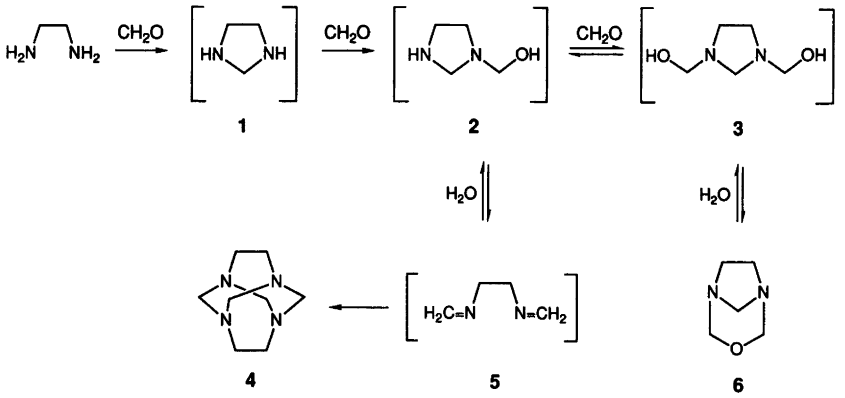
We now report a systematic study of the products obtainable from the reaction between diprimary α,ω-alkanediamines $NH_2(CH_2)_nNH_2$ (n = 2–5) and formaldehyde. The reactions were carried out with 37 % aqueous formaldehyde solutions. The addition of a stronger base (NaOH) did not change the course of the reaction. The type of condensation product turned out to be remarkably dependent on the length of the alkane chain and included in certain cases an irreversible Cannizzaro-like intramolecular rearrangement of intermediate 1,3-bis(hydroxymethyl)-1,3-diazacycloalkanes to give 1-formyl-3-methyl-1,3-diazacycloalkanes.

To examine the scope of this interesting disproportionation reaction, we extended the study to a series of disecondary alkanediamines $CH_3NH(CH_2)_nNHCH_3$ (n = 2–4). Here, the *N,N'*-bishydroxymethyl intermediates would of course be acyclic, and again the outcome depended on the length of the alkane chain.

The results will first be presented individually for each compound investigated, whereafter reasons for the dissimilar behaviour will be discussed.

Diprimary alkanediamines

1,2-Ethanediamine (Scheme 1). A Japanese patent[8] claims the isolation of the simple unicyclic compound **1** (tetrahydroimidazole). No data were reported, and we have been unable to obtain any trace of it even when using a large excess of the diamine. The main reaction products we



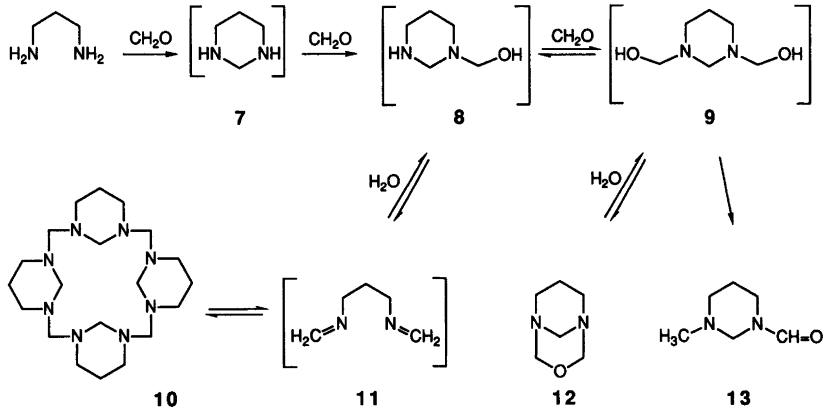
Scheme 1.

were able to isolate by distillation and crystallization were the same bicyclic oxadiaza compound **6** and tricyclic tetraaza compound **4**, with tertiary amino nitrogen only, as reported in the literature.[3,4,6] The ratio changed little with reaction time, or by addition of NaOH, although it has been stated[6] that the formation of **6** is catalysed by NaOH. As expected, a great excess of formaldehyde (in water) favours somewhat the oxygen-containing bicycle **6**, whereas the use of gaseous formaldehyde and liquid diamine favours the tricycle **4**.

Reaction paths are proposed in Scheme 1. The bis-hydroxymethyl compound **3**, although not observed, is the obvious precursor for the bicycle **6**. This is easy to isolate and a suitable candidate for our alkylation studies, which will be reported separately. A bis-imine intermediate **5** is proposed as the precursor which by dimerization gives the tricycle **4**. Compounds **1** and **2** are excluded as direct precursors since their five-ring structure is not retained in the tricyclic structure **4**. This can best be described as a 1,3,5,7-tetraazacyclooctane carrying two transannular ethylene bridges, and is completely analogous to the structure of hexamethylenetetramine (two methylene bridges). In agreement with the X-ray structure,[5] the D_{2d} symmetry of **4** is proved by the presence of only two ^{13}C NMR signals and two ^{1}H singlets.

1,3-Propanediamine (Scheme 2). The simple unicyclic compound **7** (hexahydropyrimidine) was also present in insufficient quantity to be observed. The distilled product consisted of an irreversibly formed substance the ^{1}H and ^{13}C NMR spectra of which identified it as the *cis,trans*-isomeric mixture of 1-formyl-3-methylhexahydropyrimidine **13**, accompanied after short reaction times by the bicyclic oxadiaza compound **12**. The formamide **13** could be obtained pure by preparative gas chromatography, whereas the bicycle **12** decomposed. After our independent observation, exactly the same reaction was reported, but for this diamine only, by Bagga *et al.*[7]

We propose (Scheme 2) that the formamide **13** arises by hydride shift from the bis-hydroxy-methylated precursor **9**. The reason that the bicycle **12**, which is formed first, does not accumulate, must be that it is in fast equilibrium with the same precursor **9**. After long reaction times the formamide **13** becomes the exclusive product, and we are quite unable to explain how Krässig,[4] and later Evans,[9] could fail to observe this stable end product. The intramolecular nature of the hydride shift is proved by the complete absence of the dimethyl or diformyl derivative of hexahydropyrimidine. In the chair conformation of the six-membered ring of **9**, the two hydroxymethyl substituents can come close enough when both are axial. This is not possible in the



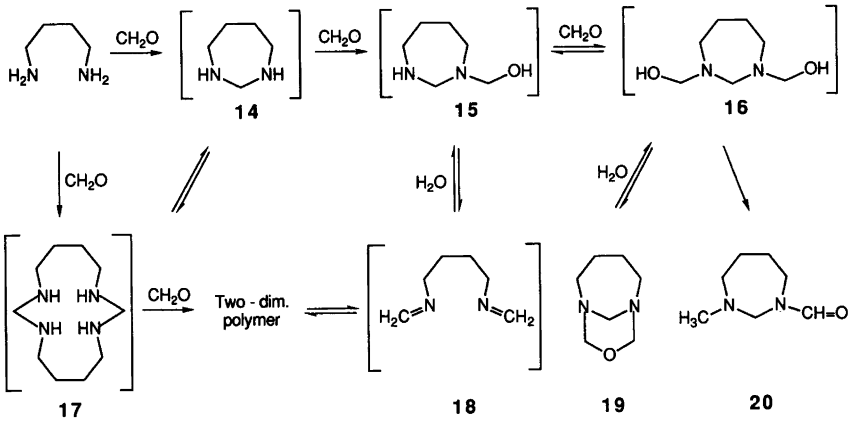
Scheme 2.

more flattened five-membered ring of the tetrahydroimidazole **3** and no hydride shift can occur.

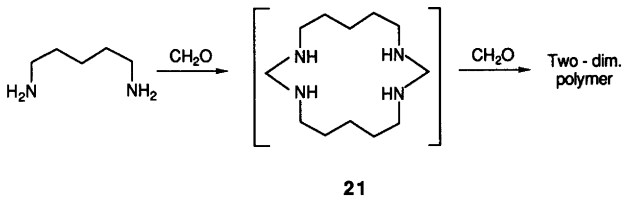
Using short reaction times a sizeable residue remains after distillation. When water is added, a crystalline solid precipitates, as already reported by Krässig[4] and correctly assigned the quinquecyclic 'tetrameric' structure **10**, later confirmed by Evans.[9] In full agreement, the ^{13}C NMR spectrum of freshly dissolved crystals showed, at room temperature, the presence of a single species with two types of NCH_2N group, 1:1. The ^1H NMR spectrum was very complex and changed dramatically and reversibly with temperature, suggesting one, or more, rigid, well defined conformations. A thorough DNMR study, as well as an X-ray structure determination, are reported in the following paper. Compound **10** is thermally unstable and solutions develop new sets of ^{13}C lines with time at high temperature. Attempts to obtain the mass spectrum by chemical ionization and even by field ionization or field desorption (normally not expected to produce fragmentation) gave predominantly the masses 98 and 99, corresponding to *M* and *M* + 1 for the bis-imine **11**, accompanied by much weaker *M* + 1 mases for 'dimer', 'trimer', and the initial 'tetramer' **10**. Thus, rapid and almost complete pyrolysis takes place faster than volatilization of the sample. This pyrolysis may simply be the reversal of a possible mode of its formation from **8** via **11**.

1,4-Butanediamine (Scheme 3). When aqueous formaldehyde was added to a solution of 1,4-butanediamine in CH_2Cl_2, the organic phase was seen by NMR spectroscopy to contain a mixture of the bicyclic oxadiaza compound **19** and the formamide **20**, both presumably formed from the bis-hydroxymethylated unicyclic precursor **16**. After some days only the formamide was present, suggesting reversibility between **16** and **19**. After prolonged standing, the isolated liquid seven-ring formamide **20** became transformed into a hard, glass-clear polymer, presumably of linear ring-opened structure, since it was soluble in organic solvents. On the other hand, the addition of formaldehyde to 1,4-butanediamine in concentrated aqueous solution caused rapid precipitation of a white solid, insoluble in both polar and non-polar solvents. Attempts to pyrolyse this solid produced only a small amount of the formamide **20**. The same reaction in dilute aqueous solution gave first a rapid precipitation of the polymer, which, however, on being stirred further passed slowly into solution to give, after work-up, the formamide **20** as the exclusive product. We believe initially precipitated polymer to consist of tetraazacyclotetradecane rings **17** interconnected by CH_2-bridges, resulting in a two-dimensional insoluble polymer. Interconnection of diazacycloheptane rings **14** with formaldehyde should lead to a linear polymer with good solubility. The elemental analysis is correct for $(C_6H_{12}N_2)_x$ as expected for both structures, and solid-phase ^{13}C NMR spectroscopy confirmed only the presence of three types of CH_2 group with the expected shifts for $CH_2CH_2CH_2$, CH_2CH_2N and NCH_2N and the absence of C linked to O. Equilibria between monomeric 7-ring and dimeric 14-ring compounds are well established, for example for analogous 1,3-dioxa compounds.[10,11] Thus, the initial polymer is in mobile equilibrium, through more or less hydroxymethylated derivatives of **17** and **14**, with the precursor **16** for the irreversible rearrangement to the formamide **20**, and further to the final glassy polymer. Alternatively, the bis-imine **18** may be a direct precursor for the initial polymer, and reformed from it in the reverse reaction.

1,5-pentanediamine (Scheme 4). In this case there was again rapid precipitation of a polymer, but in contrast with the precipitated polymer from 1,4-butanediamine, it did not redissolve in water and no low-molecular-weight product was formed on standing, with elevated temperatures, or even under pyrolytic conditions. It thus seems that a bis-hydroxymethyl-1,3-diazacyclooctane intermediate, presumed by analogy with the previous cases to be necessary for the rearrangement to the 1-formyl-3-methyl derivative, is not present because of medium-ring strain. The 'dimeric' tetraazacyclohexadecane **21** is therefore the smallest unstrained ring, as found for the corresponding 1,3-dioxa compounds.[11,12] Again, we believe that the polymer is formed by further condensation with formaldehyde to give a two-dimensional network consisting of CH_2-intercon-



Scheme 3.



21

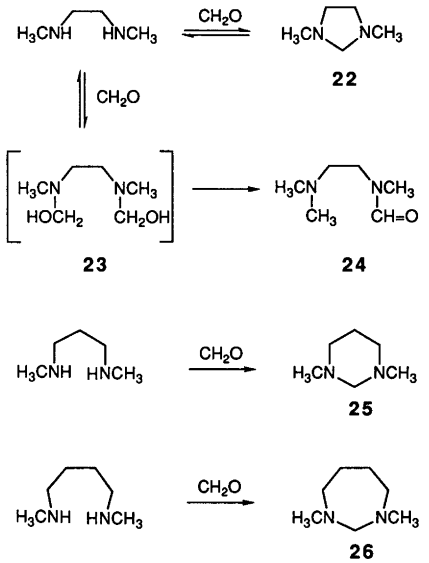
Scheme 4.

nected macrocycles. The elemental analysis $(C_7H_{14}N_2)_x$ and the solid-phase ^{13}C NMR spectrum are again in agreement with such a structure.

We postulate that, for conformational reasons, neither the present 16-ring intermediate nor the previous 14-ring intermediate can undergo intramolecular hydride shift after *N*-hydroxymethylation. This will be discussed in further detail below.

Disecondary alkanediamines

N,N′-*Dimethyl-1,2-ethanediamine (Scheme 5).* The simple unicyclic compound **22** (1,3-dimethyltetrahydroimidazole) was quickly formed when aqueous formaldehyde was added, but was slowly converted into the acyclic *cis,trans*-isomeric formamide mixture **24**, presumably through the unobserved bis-hydroxymethylated precursor **23**. Again, the hydride shift is clearly intramolecular, since no tetramethyl or diformyl-dimethyl derivative was observed. Mixtures of **22** and **24** could be separated by fractional distillation. In no case did we observe the presence of a 'dimeric' cyclization product, 1,3,6,8-tetramethyl-1,3,6,8-tetraazacyclodecane, as reported by Krässig,[4] who claims to have separated it from the 'monomer' **22**, but gives no mention of the formamide **24**. Ten-membered rings are generally disfavoured by medium-ring strain, and the easy interconversion of such aminal mixtures would, during the distillation, allow a continuous displacement of the equilibrium in favour of the more volatile five-ring component **22**.



22 23 24 25 26

Scheme 5.

N,N′-*Dimethyl-1,3-propanediamine.* The only observed product here was the unicyclic compound **25** (1,3-dimethylhexahydropyrimidine). No 'dimeric' cyclization product, 1,3,7,9-tetramethyl-1,3,7,9-tetraazacyclododecane, as reported by Krässig,[4] was obtained. The absence of this 'doubling' product parallels the absence of a 'doubling' product at room temperature for the corresponding acetals, 1,3-dioxanes.[13] The additional absence of the rearranged formyl derivative can be understood on a conformational basis (see below).

N,N′-*Dimethyl-1,4-butanediamine.* NMR spectroscopy revealed a complex mixture of products, which could not be separated by Kugelrohr distillation. The expected set of lines for the unicyclic product **26** were present, but a second set due to the 'doubling' product (which would now be a strain-free 14-membered ring) were not identified. Also, there were no lines for the rearrangement product, the formamide.

Discussion

In all the condensation reactions, end products that are not the result of rearrangement are aminals and carry exclusively tertiary amino functions; no NH groups are left and no oxygen functions are present. In some cases it is possible at the early stage to observe or trap bicyclic compounds carrying $-CH_2OCH_2-$ bridges, but as such reactions are reversible, these products never accumulate beyond a certain level.

The unique occurrence of the quinquecyclic compound **10** (Scheme 2) is particularly intriguing and requires an explanation. Only 1,3-propanediamine produces this kind of structure with the simple aminal rings **7** intact and joined together through the N-atoms by CH_2 groups to form the central polyaminal cyclic system. That just one ring size, the octaazacyclohexadecane **10**, is produced, suggests a connection with the unique ability of the six-ring and sixteen-ring skeletons not only separately to adopt perfect diamond-lattice conformations, but also to match these together into the quinquecyclic structure **10** [Fig. 1(c)]. Furthermore, full use is made of stabilizing *gauche* N···H–C interactions across all four $g^{\pm}g^{\pm}$ 'corners', the importance of similar *gauche* O···H–C interactions in 16-ring acetals having been repeatedly stressed.[11,12] During the condensation, the growing chain will have its conformation uniquely defined as shown in Fig. 1, with diequatorial substituents on the 6-ring and CH_2 groups on $g^{\pm}g^{\pm}$ 'corners'. Neither the linear 'dimer' (a) nor the 'trimer' (b) can cyclize, whereas the 'tetramer' can hardly escape cyclization (c). The conformation (c) of symmetry D_{2d} is identical with the only one present in CH_2Cl_2 and found in crystals from CH_2Cl_2 (see the following paper). A closely related S_4

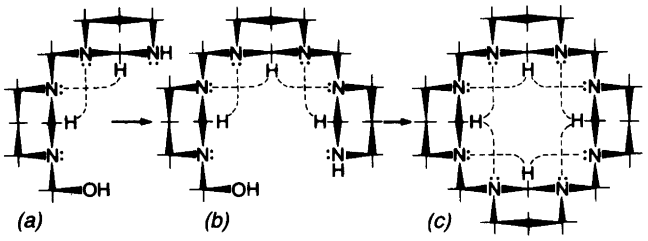


Fig. 1. Preferred conformations for linear 'dimeric' and 'trimeric' intermediates (a) and (b) and for the cyclic 'tetrameric' product **10** (c).

conformation is also present in toluene and found in crystals from benzene.[14]

The occurrence of an intramolecular hydride shift is also limited to certain cases. When such reactions occur, all the material will ultimately be transformed into a single product (or derived polymer) containing oxygen in the form of a formyl substituent. It is obvious that an intramolecular hydride shift must be totally dependent on the two *N*-hydroxymethyl groups being able to come into close proximity and therefore is very sensitive to variation in structure. The present discussion of the conformational factors involved can, to some extent, be based on existing knowledge of related ethers and acetals.[11] In rings of normal size, *N*-hydroxymethyl substituents, although preferentially disposed equatorially, may also occupy axial positions, and this is the means by which they can come closest to each other (Fig. 2). A sufficiently close approach can be realized in the puckered six- and seven-membered rings **9** and **16**, but not in the more flattened five-membered ring **3**. Presumably, eight-membered rings would also have suitable

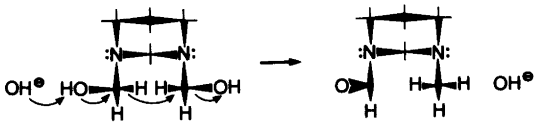


Fig. 2. Proposed mechanism for intramolecular hydride shift in the hexahydropyrimidine **9** to yield the formamide **13**.

conformations, but these are apparently not formed owing to medium-ring strain. This explains not only why the formamide compound is not formed from 1,5-pentanediamine, but also the absence of a bicyclic $-CH_2OCH-$ bridged product analogous to **6**, **12** and **19**. In macrocycles such as the 14- and 16-membered tetraaza compounds **17** and **21**, the preferred conformational unit for the 1,3-diaza groups (Fig. 3) creates a $g^{\pm}g^{\pm}$ 'corner' analogously to the corresponding macrocyclic acetals.[10,11,12] The *N*-hydroxymethyl groups will then be forced out of the ring, remote from each other, and no hydride shift can occur.

Similarly, a conformational analysis of the disecondary alkanediamines (Scheme 5) can account for the observations. If the 1,4-diaza intermediate **23** follows the analogous 1,4-dioxa system[11] with a *gauche*-preferred CH_2CH_2 bond, a conformation favourable for hydride shift becomes

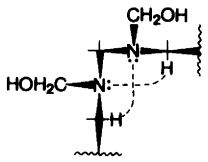


Fig. 3. Stabilized conformational 'corner' for macrocyclic compounds derived from **17** and **21**, preventing intramolecular hydride shift.

possible (Fig. 4). A 1,5-diaza intermediate, on the other hand, behaving as the analogous 1,5-dioxa compounds,[11] would have to fold the alkane chain across a $g^{\pm}g^{\pm}$ conformational 'corner' (Fig. 5), thereby orienting the *N*-hydroxymethyl groups far away from each other, and hydride shift becomes impossible.

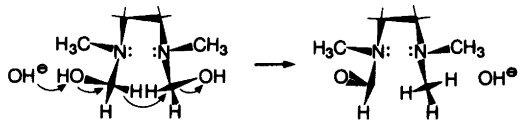


Fig. 4. Proposed mechanism for intramolecular hydride shift in the ethanediamine derivative **23** to yield the formamide **24**.

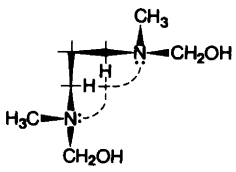


Fig. 5. Stabilized conformational 'corner' for a propanediamine derivative, preventing intramolecular hydride shift.

Experimental

Starting materials. The α,ω-alkanediamines were commercial products. The *N,N'*-dimethyl-α,ω-alkanediamines were prepared from the corresponding alkanediamines via the bis-tosylamides by a modification of Boon's procedure.[15]

A solution of *p*-toluenesulfonyl chloride (48 g, 0.25 mol) in CH_2Cl_2 (150 ml) was added dropwise to a stirred, ice-cooled solution of the alkanediamine (0.1 mol) and NaOH (10 g, 0.4 mol) in water (100 ml). The mixture was left with stirring at room temperature overnight, then poured on to a mixture of ice (100 g) and conc. HCl (32 ml). After work-up, the crude bis-tosylamides were recrystallized from methanol–ethanol (1:1). Yields and m.p.: n = 2, 87%, 156–161 °C; n = 3, 84%, 144–146 °C; n = 4, 93%, 142–144 °C.

To a stirred solution of the bis-tosylamide (25 mmol) in refluxing abs. ethanol (40 ml) was added a solution of sodium ethoxide (50 mmol) in abs. ethanol (40 ml). After 1 h of reflux, the mixture was cooled and the precipitated salt

filtered off. This disodium salt of the bis-tosylamide (67 mmol) was then dissolved in DMF (200 ml) and dimethyl sulfate (150 mmol) added dropwise with stirring, and the solution then left at room temperature for 12 h. Water (400 ml) was then added, and the precipitation completed by leaving the solution for 1 h in the refrigerator. The crude *N,N'*-dimethyl-bis-tosylamide was filtered off and recrystallized from ethanol–methanol (1:1). Yields and m.p.: n = 2, 77 %, 167–170 °C; n = 3, 90 %, 117–120 °C; n = 4, 82 %, 134–135 °C.

A suspension of the *N,N'*-dimethyl-*N,N'*-ditosyl-α,ω-alkanediamine (30 mmol) and conc. H_2SO_4 (24 g, 245 mmol) in water (5 ml) was stirred at 90–100 °C overnight. After cooling, water was added until all solids dissolved, and the solution was made alkaline with solid NaOH and steam-distilled. The distillate was acidified with conc. HCl and the water evaporated. The solid bis-hydrochloride was dissolved in a minimum quantity of water and saturated with solid NaOH. The *N,N'*-dimethyl-α,ω-alkanediamine separated as a liquid phase, which was dried over NaOH and distilled. Yields and b.p.: n = 2, 48 %, ca. 108 °C; n = 3, 86 %, ca. 140 °C; n = 4, 75 %, ca. 160 °C.

Attempts to apply newer methods via bis-trifluoroacetamide formation,[16] or via bis-imine formation with benzaldehyde,[2] were unsuccessful.

Condensation reactions

1,2-Ethanediamine. To a stirred solution of 1,2-ethanediamine (60 g, 1 mol) in water (100 ml), kept below 40 °C by ice cooling, was added dropwise, over 1 h, 37 % aqueous formalin (243 g, ca. 3 mol). The mixture was stirred for 18 h at room temperature. Volatile components were distilled out of the mixture (bath temp. 100 °C/20 mmHg), to leave a white solid residue of *1,3,6,8-tetraazatricyclo[4.4.1.1^{3,8}]dodecane* **4**, which could be recrystallized from dioxane. Yield 56.3 g (67 %), m.p. 190–210 °C (lit.[17] 198–211 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.25 (8 H, s), 3.96 (8 H, s). ^{13}C NMR (75 MHz, $CDCl_3$): δ 58.5 (CCH_2N), 73.7 (NCH_2N).

The distillate was extracted with $CHCl_3$ (5×125 ml) and the $CHCl_3$ solution dried (Na_2SO_4) and evaporated. Distillation of the residue gave *3-oxa-1,5-diazabicyclo[3.2.1]octane* **6** as a soft solid. Yield 9.8 g (9 %), b.p. 40–50 °C/14 mmHg (lit.[6] m.p. 98 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.91 (2 H, m), 3.25 (2 H, m), ca. 3.3 (1 H), ca. 4.3 (1 H, d, J 9.3 Hz), 4.27 (2 H, J 10.4 Hz), 4.77 (2 H, d, J 10.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 51.2 (CCH_2N), 75.2 (NCH_2N), 87.2 (NCH_2O).

1,3-Propanediamine. The procedure described above, applied to 1,3-propanediamine, gave a distillation residue which crystallized by addition of water. Recrystallization from dioxane gave *1,3,7,9,13,15,19,21-octaazaquinquecyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosane* **10**.* Yield 37.2 g (76 %), m.p. 161–168 °C (lit.[9] 165–168 °C). ^{1}H NMR (300 MHz, $CDCl_3$): broad abs. regions, temp. variable (see following paper). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.7 (CCH_2C), 51.6 (CCH_2N), 72.0 (NCH_2N), 75.0 (NCH_2N).

The distillate gave an inseparable mixture of two compounds as shown by GLC. One of the compounds could be obtained pure by preparative GLC and proved to be *1-formyl-3-methyl-1,3-diazacyclohexane* **13**. Yield 10.2 g (16 %), b.p. 100–105 °C/8 mmHg. The NMR spectrum revealed the presence of two sets of lines (*cis* + *trans*) in the ratio 2:3. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27 (2 H, m), 1.88 + 1.89 (3 H, s), 2.48 (2 H, m), 2.98 + 3.10 (2 H, t, J 5.5 + 5.9 Hz), 3.48 + 3.64 (2 H, s), 7.63 + 7.67 (1 H, s). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.7 + 23.7 (C-5), 38.6 + 44.4 (C-6), 41.0 + 41.2 (NCH_3), 53.8 + 5.41 (C-4), 62.2 + 68.6 (C-2), 160.3 + 160.4 (CH=O).

The extra lines present in the spectrum of the freshly distilled product could be attributed to *3-oxa-1,5-diazabicyclo[3,3,1]nonane* **12**. ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.6 (CCH_2), 51.5 (CCH_2N), 69.8 (NCH_2N), 84.8 (NCH_2O).

The compound decomposed upon attempted isolation by preparative GLC. The ratio between the volatile products **12** and **13** as a function of reaction time was monitored by GLC. After 1 h **12** was the major component (2:1), but **13** became the exclusive product after 9 days.

1,4-Butanediamine. To a stirred and ice-cooled solution of 1,4-butanediamine (8.8 g, 0.1 mol), with or without NaOH (0.4 g), in water (10 ml) was added dropwise 37 % formalin. A white solid precipitated; it was filtered off and washed with water, and was insoluble in both polar and non-polar solvents. The material was dried under vacuum until constant weight was achieved. Yield 8 g (56 %). Anal. $(C_6H_{12}N_2)_x$: Found: C 64.2, H 10.9. Calc.: 64.3; H 10.7. ^{13}C solid-phase NMR (50 MHz): δ ca. 25 (CCH_2C), ca. 52 (CCH_2N), ca. 74 (NCH_2N).

Pyrolysis yielded a small amount of *1-formyl-3-methyl-1,3-diazacycloheptane* **20**, as a *cis,trans*-isomeric mixture. Anal. $C_7H_{14}N_2O$: C, H, N, O. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.66 + 1.81 (4 H, m), 2.26 + 2.37 (3 H, s), 2.77 (2 H, t, J 5.1 Hz), 3.43 (2 H, t, J 5.9 Hz), 4.22 + 4.26 (2 H, s), 8.10 + 8.13 (1 H, s). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.6 and 25.9 (C-5 + C-6), 38.4 (CH_3N), 44.1 (C-4), 56.4 (C-7), 68.0 (C-2), 163.1 (CH=O).

The proportion of **20** could be increased by performing the condensation in a larger volume of water, which prevented the precipitation of the polymer, and by using long reaction times (18 h). Extraction with $CHCl_3$ yielded the formamide **20** as the main product. Yield 57 %, b.p. 116–120 °C/8 mmHg.

Using a two-phase system, H_2O–CH_2Cl_2, the product passed continuously into the organic phase and consisted after a short reaction time of a mixture of the formamide **20** and *8-oxa-1,6-diazabicyclo[4.3.1]decane* **19**. After longer reaction times, compound **19** was converted into **20**. Liquid

* IUPAC recommended name: 1,3,7,9,13,15,19,21-octaazapentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosane.

samples of the formamide **20** changed within days to a glass-clear solid, soluble in solvents such as CH_2Cl_2.

1,5-Pentanediamine. When 37% aqueous formalin was added dropwise to a stirred and ice-cooled solution of 1,5-pentanediamine in water, a white solid precipitated immediately which was insoluble in both polar and non-polar organic solvents. The solid did not redissolve in water, even after long reaction times, and did not produce a formamide by rearrangement either in solution or by pyrolysis. The solid was dried under vacuum until constant weight. Yield 87%. Anal. $(C_7H_{14}N_2)_x$: Found: C 65.9; H 11.0. Calc. C 66.7; H 11.1. ^{13}C solid-phase NMR (50 MHz): δ ca. 25 (CCH_2C), ca. 51 (CCH_2N), ca. 72 (NCH_2N).

N,N′-*Dimethyl-1,2-ethanediamine.* To a stirred and ice-cooled solution of *N,N′*-dimethyl-1,2-ethanediamine (2.2 g, 25 mmol) in water (10 ml) was added dropwise 37% aqueous formalin (4.05 g, 50 mmol formaldehyde) and the mixture stirred at room temp. for 18 h. The $CHCl_3$ extract was dried (Na_2SO_4) and the $CHCl_3$ evaporated. Distillation at 10 mmHg gave one fraction, b.p. 40–70°C, the NMR spectrum of which corresponded to impure *1,3-dimethyl-1,3-diazacyclopentane* **22**, and one fraction, b.p. 94–96°C, shown to be a *cis,trans*-isomer mixture of N-*formyl*-N,N′,N′-*trimethyl-1,2-ethanediamine* **24**. Yield 2.1 g (65%), b.p. 94–96°C/10 mmHg. ^1H NMR (300 MHz, CD_3CN): δ 2.19 (6 H, s), 2.35 (2 H, 2 × t, *J* 3 Hz), 2.78 + 2.90 (3 H, s), 3.28 + 3.35 (2 H, t, *J* 6.2 + 6.7 Hz), 7.95 (1 H, s). ^{13}C NMR (75 MHz, CD_3CN): δ 29.6 + 34.9 (CH_3N), 42.3 + 47.8 (C-2), 45.7 (CH_3N), 56.8 + 57.7 (C-1), 163.3 + 163.6 (CH=O).

N,N′-*Dimethyl-1,3-propanediamine.* The same procedure as above was used. Distillation of the chloroform residue gave a single fraction, identified as *1,3-dimethyl-1,3-diazacyclohexane* **25**. Yield 86%, b.p. 110–115°C/760 mmHg (lit.[9] 58–60°C/20 mmHg). ^1H NMR (300 MHz, $CDCl_3$): δ 1.70 (2 H, quintet, *J* 5.4 Hz), 2.25 (6 H, s), 2.40 (4 H, br), 2.98 (2 H, br). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.4 (C-5), 42.6 (NCH_3), 53.6 (C-4, C-6), 79.2 (C-2).

The distillation residue was examined by NMR spectroscopy and found to contain no rearranged formamide product.

N,N′-*Dimethyl-1,4-butanediamine.* The same procedure was used. Attempts to distil, in a Kugelrohr, the product extracted by $CHCl_3$ gave no fractionation into pure compounds. A set of lines in the NMR spectrum of the mixture could be assigned to *1,3-dimethyl-1,3-diazacycloheptane* **26**, but no lines could be attributed to a rearranged formamide product.

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