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Syntheses of novel *N*-[bis(trimethylsilyl)methyl]-1,2- and 1,3-diamines

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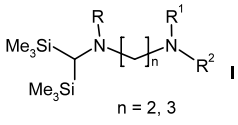
Abstract

Original *N*-[bis(trimethylsilyl)methyl]-1,2- and 1,3-diamines of type I were prepared either from bis-imination reaction of 1,2-dicarbonyl compounds with bis(trimethylsilyl)methylamine, BSMA (**1**) followed by reduction or from cyanoethylation of BSMA followed by reduction of the nitrile group. By varying the conditions of the cyanoethylation reaction bisaddition was obtained allowing to access to 5-[bis(trimethylsilyl)methyl]caldine (**8**).



I

Keywords: α-Silylamines; Polyamines; Bis-imination reactions; Cyanoethylation reactions; Caldine

1. Introduction

We have recently reported on the fascinating chemistry of bis(trimethylsilyl)methylamine (BSMA (**1**)) [1]. Among the interesting properties of BSMA's derivatives are: (a) the very high solubility of BSMA's hydrochloride in water in spite of the two trimethylsilyl groups, and its remarkable solubility in pentane (45 g/l) although being a salt; (b) the Si–C(sp^3)–N framework is recognized as a potential pharmacophore and an increasing number of derivatives have been shown to be biologically active (Fig. 1) [2].

1,*n*-Diamines and 1,*n*-diamino derivatives are very important compounds, not only in organic synthesis (mostly 1,2- or vicinal diamines) [3–8] but also in life chemistry (mostly 1,3- and 1,4-di- and polyamines) where they exist naturally in plants and animals and play an important role in the cell development [9,10].

Some polyamines having the Si–C–N framework have been reported in the literature, as diamine **G** [11] and *N,N,N′*-trimethyl-*N′*-[(trimethylsilyl)methyl]ethylene diamine (**H**) which has been obtained as a side product when tetramethylsilane has been treated successively with *n*-butyllithium/tetramethylethylene diamine complex and trimethyl-silyl chloride [12]. Series of 1,n-[*N*,*N*,*N′*,*N′*-(tetramethyl)aminomethyl]tetramethyldisila-alkanes methiodides (**I**) have been found to exhibit neuro muscular blocking activity [13]. Sila-*cis*-platine (**J**) has been shown to exert antitumor and antileukemic activities comparable to that of its carbon counterpart (Fig. 2) [14].

In the frame of our continuing efforts to develop chemistry of BSMA and taking advantage of the peculiar properties of their derivatives, we have investigated the synthesis of some 1,*n*-polyamines ($n = 2$ and 3) that have the bissilylmethyl group as a substituent at nitrogen. The aim of this work was to (a) synthesize such molecules that couple biological properties of polyamines with those related to the Si–C–N framework; (b) offer possibilities to utilize the Si–C bond for further

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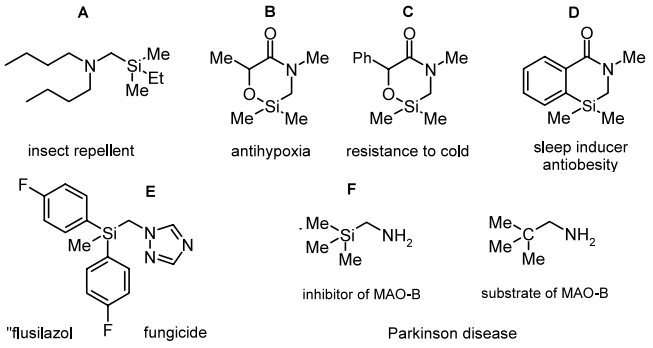


Fig. 1. Examples of SMA's bioactive compounds.

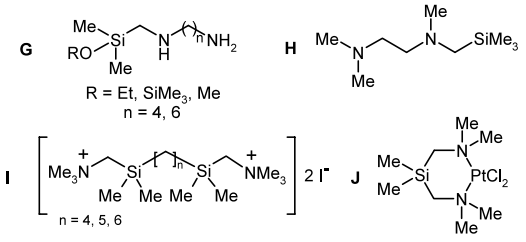


Fig. 2. SMA's polyamines in the literature.

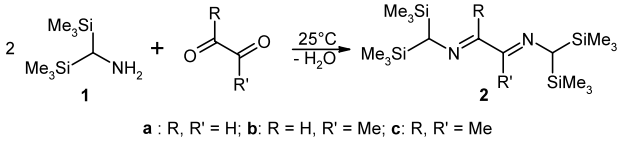
chemistry (functionalization, grafting on other organic molecules or on solid supports); (c) give better lipophilicity to molecules that are, otherwise, hydrophilic in nature.

2. Syntheses of silylated 1,2-diamines

Among the numerous synthetic ways proposed in the literature to access to vicinal diamines [3], we have chosen to condense BSMA (**1**) with 1,2-dicarbonyl compounds **2** because of the high reactivity of this amine with aldehydes and ketones [1]. Bisimines thus obtained were reduced into corresponding diamines [15].

2.1. Bisimines

Condensation of **1** with glyoxal (dissolution in water) at room temperature led to the desired diene, **2a**, with excellent yield (95%) and stereocontrol (one single isomer, exclusively *E*-*E* based on the general trend of BSMA's imines to adopt this geometry [16]; Eq. (1)).



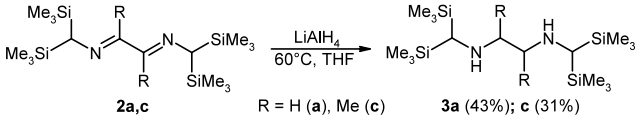
(1)

Similarly, pyruvic aldehyde gave the corresponding diene, **2b** as a single isomer (*E*-*E*) in 82% yield (Eq. (1)).

In both cases, although water is formed during the reaction, insolubility of **2a** and **2b** in water shifts the equilibrium. With diacetyl as the dicarbonyl starting material, a desiccant (4 Å molecular sieves) in dichloromethane has to be used to get the diene **2c** as a single isomer (*E*-*E*) in 55% yield (Eq. (1)).

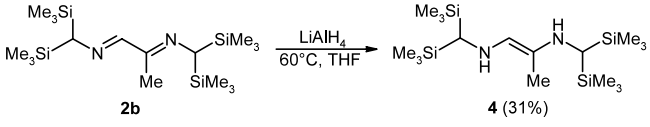
2.2. Diamines

Bisimines **2a**,**c** were easily reduced into the corresponding vicinal diamines **3a**,**c** with lithium aluminum hydride (LAH) in THF under reflux. Their lengthy and difficult extractions are probably at the origin of the medium yields obtained (Eq. (2)).



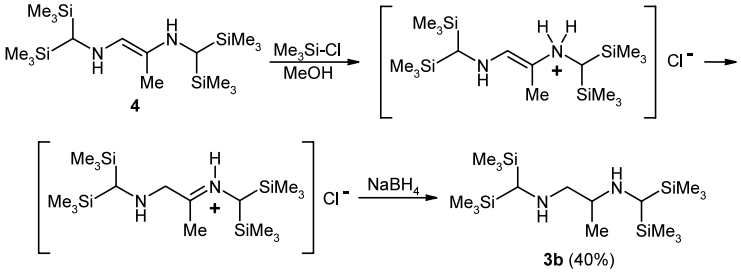
(2)

Treatment of **2b** in the same conditions did not lead to **3b**, but to the enediamine **4** instead, as a single isomer (Eq. (3)).



(3)

Following a procedure used to reduce enamines into amines [17], this enediamine was transformed into its



(4)

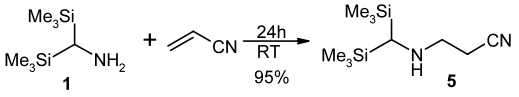
hydrochloride with one equivalent of trimethylchlorosilane in methanol solution. This salt was then reduced with sodium borohydride to give the corresponding vicinal diamine **3b** in 40% yield (Eq. (4)).

3. Syntheses of silylated 1,3-di- and triamines

Addition of primary and secondary amines to ethylenic substrates having a withdrawing group is a well-known reaction that gives access to β-functionalized amines. We have used this strategy to synthesize 1,3-diamines with **1** as the amine.

3.1. Syntheses of nitriles

First attempts were made with **1** dissolved in acrylonitrile. After 24 h at room temperature, the 1:1 adduct **5** was obtained in quantitative yield. No 1:2 adduct was observed that could have resulted from a double addition (Eq. (5)).



(5)

Vögtle and coworkers [18] have described an efficient synthesis of dendrimeric polyamines based on successive polycyanoethylation of amines and nitrile reduction reactions. A large excess of acrylonitrile with a 1:1 mixture of amine and acetic acid was employed. Using these conditions, condensation of **1** with acrylonitrile was reconsidered both at low (20 °C) and high (80 °C) temperature.

As indicated by GC analysis during the reaction at low temperature, only **5** was formed and yield was not better than ~80%. At this point, quantitative yield was obtained by heating the reaction mixture at 60 °C for 4 h (Fig. 3).

Reaction performed at high temperature was more complex as monoadduct **5** and bisadduct **6** were formed. BSMA (**1**) was entirely consumed after 24 h, then started the formation of **6**. After 80 h, reaction medium was very viscous due to polymerization of acrylonitrile[1] (Fig. 4).

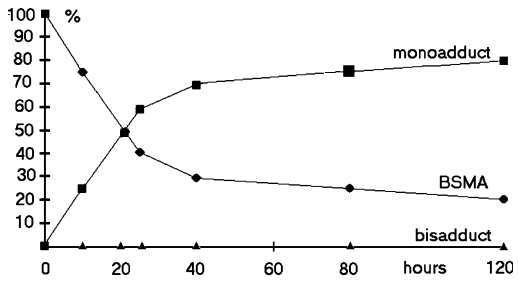


Fig. 3. Monoaddition of **1** to acrylonitrile (20 °C).

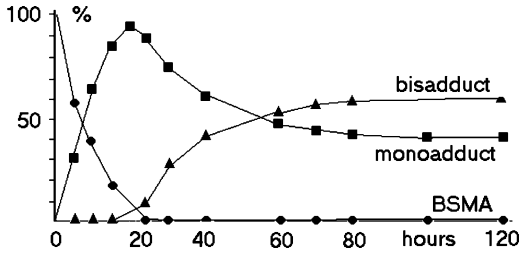
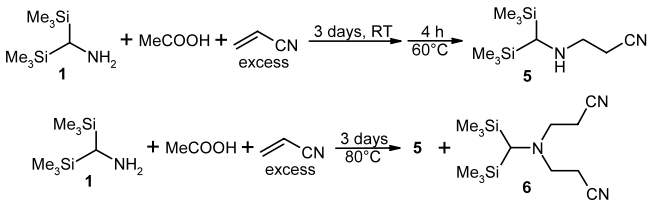


Fig. 4. Diaddition of **1** to acrylonitrile (60 °C).

The adducts were easily separated and the monoadduct recycled following the same protocol (Eq. (6)).



(6)

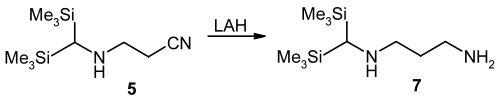
Cyanoethylation reaction of amines is generally accepted as a nucleophilic addition of the amine to the double bond of acrylonitrile. Vögtle and coworkers [18] did not give any information why they used acetic acid in equimolar amount with respect to the amine. It is well known, however, that acrylonitrile polymerization may be initiated with Lewis bases such as amines. Thus, it may be anticipated that use of acid limited concentration of nucleophilic species present in the reaction medium and able to initiate polymerization.

In the present work, we have observed that addition of **5** to acrylonitrile was more difficult than that of **1**. This could be explained by the presence of polyacrylonitrile, which made reaction medium less and less homogeneous. Basicity of **5** greater than that of BSMA has also to be taken into account. So, we believe that effectively the role of acetic acid was to keep lower as possible the concentration of amines (**1** and **5**), which were released from their ammonium acetates as the reaction progressed.

3.2. Synthesis of amines

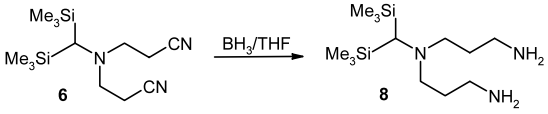
Mononitrile **5** was easily converted into the corresponding original primary amine **7** using LAH in diethyl ether. Moderate yields were obtained, probably because of the difficult recovery of the product during the work-up (Eq. (7)).

[1] In spite of the presence of added 4-methoxyphenol (MEHQ) and the use of degazed acrylonitrile.



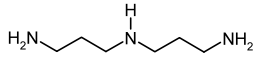
5 7 (7)

The same procedure applied to dinitrile **6** has been ineffective, not because of failure of the reaction but because it was very difficult to recover the formed amine. Borohydride reduction in the presence of cobalt chloride [18] also failed, even when extraction from the work-up residue was attempted in the presence of triethanolamine [19] which was supposed to be a better chelating agent than the expected triamine **8**. Finally, this amine was obtained in moderate yield by treating **6** with BH_3/THF complex [20] followed by hydrolysis with 6 N hydrochloric acid (Eq. (8)).



6 8 (8)

This triamine can be considered as deriving from caldine or norspermidine [bis(3-aminopropyl)amine], a natural polyamine [10] by substituting the bis(trimethylsilyl)methyl group on the central nitrogen atom for the proton.



caldine (norspermidine)

4. Conclusions

Original 1,2- and 1,3-polyamines has been easily synthesized. These syntheses illustrate the good reactivity and great utility of BSMA to form bisimines from diketones or to give β-aminonitrile and β-aminodinitrile via cyanoethylation reaction.

5. Experimental

5.1. General

^{1}H-NMR spectra were recorded on a Perkin–Elmer Hitachi R-24B (60 MHz) and a Brucker AC 250 (250.133 MHz) with chloroform as internal standard and deuterated chloroform as the solvent. Chemical shifts (δ, ppm) are given from TMS and coupling constants are in absolute value. To describe spectra the following abbreviations were used: s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet or complex massif).

^{13}C-NMR spectra were recorded on a Brucker AC 200 (50.32 MHz) and 250 (62.89 MHz) with $CDCl_3$ as the internal reference ($\delta = 77.39$ ppm/TMS). Solvent used is given with the description of the products. Peak multiplicity was determined by GASPE (gated spin echo) and DEPT (distortionless enhancement by polarization transfer).

IR spectra were registered (net liquids or KBr pellets for solids) on a Perkin–Elmer 457, Perkin–Elmer IRFT Paragon 1000 or Nicolet 20 SXC GC (Fourier transform) fitted with a Carlo Erba GC 6000 Vega (PTE 5 capillary column, 25 m, 0.25 μm).

Mass spectra were recorded on a VG Micromass 16F (70 eV, simple focalization) equipped with a Data System 2040 and connected to a Intersmat IGC 121M GC apparatus (capillary column, BP1, 25 m, 0.25 μm).

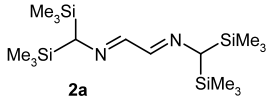
BSMA (**1**) was prepared following published procedures [17,21]. Other chemicals and solvents were commercially available and used as received.

5.2. Vicinal bisimines

Amine **1** (2 g, 11.4 mmol) was placed in a round-bottomed flask with a stirring bar. Then glyoxal (40% aqueous solution, 0.82 g, 5.7 mmol) was slowly added via syringe at room temperature and the mixture was kept under stirring for 4 h. The emulsion was extracted with ether (3×20 ml). Ether solution was dried over anhydrous magnesium sulfate. Filtration and evaporation of the solvent left a white solid, which was recrystallized in methanol. These bisimines have the *E-E* configuration.

5.2.1. (*E,E*)-*N,N′*-[Bis(trimethylsilyl)methyl]-1,2-diiminoethane (**2a**)

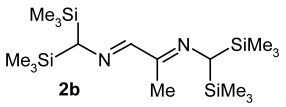
M: 372. 95% yield. ^{1}H-NMR: δ 0.00 (s, 36H), 2.74 (s, 2H), 7.69 (s, 2H) ppm. ^{13}C-NMR ($CDCl_3$): δ −1.3 ($SiMe_3$), 60.8 ($NCHSi_2$), 158.8 ($CH{=}N$) ppm. IR (cm^{-1}) 2741 (CH=), 1593 (C=N), 1248 and 840 ($SiMe_3$). MS (EI); *m/z*: 372 (12.2), 357 (18.2), 299 (100), 73 (71.1).



2a

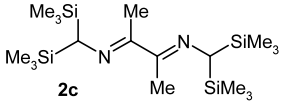
5.2.2. (*E,E*)-*N,N′*-[Bis(trimethylsilyl)methyl]-1,2-diiminopropane (**2b**)

M: 386. 82% yield. ^{1}H-NMR: δ −0.01 (s, 18H), 0.00 (s, 18H), 1.87 (s, 3H), 2.74 (s, 1H), 7.61 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$): δ −1.3 ($SiMe_3$), −1.1 ($SiMe_3$), 11.6 ($H_3CC{=}N$), 51.6 ($NCHSi_2$), 58.8 ($NCHSi_2$), 160.9 ($CH{=}N$), 162.6 ($C{=}N$) ppm. IR (cm^{-1}) 2752 (CH=), 1610 (C=N), 1248 and 841 ($SiMe_3$) ppm. MS (EI); *m/z*: 386 (10.6), 371 (18.3), 313 (100), 73 (75.2) ppm.



*5.2.3. (E,E)-N,N′-[Bis(trimethylsilyl)methyl]-2,3-diiminobutane (**2c**)*

M: 400. 55% yield. m.p.:137 °C. ^{1}H-NMR: δ 0.00 (s, 36H), 1.97 (s, 6H), 3.12 (s, 2H) ppm. ^{13}C-NMR ($CDCl_3$): δ −1.2 ($SiMe_3$), 11.1 (H_3CC=N), 50.7 (N*C*HSi_2), 163.0 (*C*=N) ppm. IR (cm^{-1}): 1610 (C=N), 1248 and 847 ($SiMe_3$).

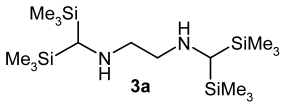


5.3. Vicinal diamines

In a flame-dryed, round-bottomed flask was placed freshly distilled THF (20 ml) under dry nitrogen gas and the flask was placed in a ice-bath. Then, LAH (0.4 g, 10.5 ml) was slowly added under stirring and 4 mmol of **2** dissolved in THF (10 ml) were introduced drop by drop. After stirring for 3 h at room temperature, the flask was maintained in an ice-bath and successively iced water, 15% aqueous sodium hydroxide and water were added. Filtration over celite, evaporation of THF left a residue which was taken up with chloroform. Organic phase was washed with water, dried over anhydrous magnesium sulfate, filtrated and chloroform was evaporated leaving a residue which was almost pure.

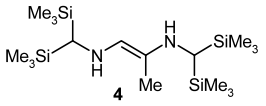
*5.3.1. N,N′-[Bis(trimethylsilyl)methyl]-1,2-diaminoethane (**3a**)*

M: 376. 43% yield. ^{1}H-NMR: δ 0.00 (s, 36H), 1.25 (s, 2H), 1.50 (s, 2H, deuterium exchangeable), 2.60 (s, 4H) ppm. ^{13}C-NMR ($CDCl_3$): δ −0.5 ($SiMe_3$), 39.7 (N*C*HSi_2), 54.3 (CH_2) ppm. IR (cm^{-1}) 3313 (NH_2), 1250 and 838 ($SiMe_3$). MS (EI); *m*/*z*: 376 (0), 361 (5.3), 303 (7.4), 188 (87.0), 73 (100).



*5.3.2. N,N′-[Bis(trimethylsilyl)methyl]-1,2-diaminopropene (**4**)*

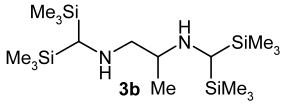
M: 388. 31% yield. ^{1}H-NMR: δ 0.06 (s, 18H), 0.11 (s, 18H), 1.95 (d, 3H, $^{4}J = 1.2$), 2.40 (s, 1H), 3.40 (s, 1H), 5.80 (q, 1H, $^{4}J = 1.2$) ppm. ^{13}C-NMR ($CDCl_3$): δ −2.7 ($SiMe_3$), −1.8 ($SiMe_3$), 11.2 (CH_3), 33.1 (N*C*HSi_2), 34.3 (N*C*HSi_2), 103.8 (*C*H=C) 115.1 (CH=*C*) ppm. IR (cm^{-1}) 3312 (NH), 1248 and 840 ($SiMe_3$).



Enediamine **4** (0.62 g, 1.6 mmol) dissolved in 15 ml methanol, was introduced in a round-bottomed flask equipped with a stirring bar, a nitrogen gas inlet and a pressure-equalizing funnel, and protected from moisture with a potassium pellets tube. Trimethylchlorosilane (0.2 g, 1.75 mmol) was added via syringe and the mixture was stirred for 1 h at room temperature. Then, volatile compounds were removed on a rotatory evaporator. Solid residue (0.68 g) was slowly added to a suspension of sodium borohydride (0.15 g, 4 mmol) in anhydrous diethyl ether (20 ml) kept in an ice-bath and protected from moisture. Stirring was maintained for 24 h leaving temperature to return to ambient. Hydrochloric acid (3.5% in water) was used to hydrolyze reaction mixture until pH 3–4 was reached. Organic impurities were extracted with ether (3 × 15 ml) and aqueous phase was made basic with sodium hydroxide pellets. Extraction with ether (3 × 20 ml), drying over magnesium sulfate, filtration and evaporation of solvent left the desired diamine **3b** (0.25 g, 40% yield)) as an orange-yellow oil.

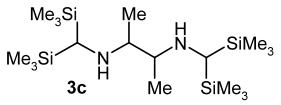
*5.3.3. N,N′-[Bis(trimethylsilyl)methyl]-1,2-diaminopropane (**3b**)*

M: 390. 40% yield. ^{1}H-NMR: δ 0.00 (s, 18H), 0.08 (s, 18H), 0.86 (d, 3H, $^{3}J = 7$), 1.17 (s, 2H), 1.19 (s, 2H), 1.25 (s, 2H, deuterium exchangeable), 2.45 (m, 1H), 2.60 (m, 2H) ppm. ^{13}C-NMR ($CDCl_3$): δ −0.8 ($SiMe_3$), −0.2 ($SiMe_3$), 18.7 (CH_3), 35.0 (N*C*HSi_2), 39.5 (N*C*HSi_2), 55.4 (CH_2), 61.1 (*C*HMe) ppm. IR (cm^{-1}) 3308 (NH), 1249 and 840 ($SiMe_3$). MS (EI); *m*/*z*: 390 (0), 375 (9.3), 317 (2.3), 202 (100), 73 (55).



*5.3.4. N,N′-[Bis(trimethylsilyl)methyl]-2,3-diaminobutane (**3c**)*

M: 404. 31% yield. ^{1}H-NMR: δ 0.00 (m, 36H), 0.82 (m, 6H), 1.19 (s, 2H), 1.62 (s, 2H, deuterium exchangeable), 2.56 (m, 2H) ppm. ^{13}C-NMR ($CDCl_3$): δ −1.3 ($SiMe_3$), −1.1 ($SiMe_3$), 13.9 (CH_3), 14.4 (CH_3), 36.6 (N*C*HSi_2), 36.7 (N*C*HSi_2), 58.4 (*C*HMe), 60.1 (*C*HMe) ppm.



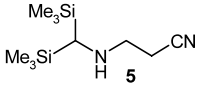
3c

5.4. Cyanoethylation of BSMA (1) at room temperature

Acrylonitrile (100 ml, stabilized with 35–45 ppm; methoxy-hydroquinone, MEHQ); glacial acetic acid (1.44 g, 24 mmol) and BSMA (4.2 g, 24 mmol) were introduced in a round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser and the mixture stirred at room temperature for 40 h and 4 h at reflux. Evaporation of the low boiling materials left an orange-yellow oil which was dissolved in chloroform (to remove traces of polyacrylonitrile) and washed with aqueous ammoniac until neutrality. Drying over magnesium sulfate, filtration and chloroform evaporation left a residue, which was purified by distillation.

5.4.1. N-[Bis(trimethylsilyl)methyl]-3-aminopropionitrile (5)

M: 228. 82% yield. b.p.: 80 °C (8 Torr). ^{1}H-NMR: δ 0.0 (s, 18H), 1.0 (s, 1H, deuterium exchangeable), 1.3 (s, 1H), 2.37 (t, 2H, $^3J = 6.7$), 2.73 (t, 2H, $^3J = 6.7$) ppm. ^{13}C-NMR ($CDCl_3$): δ −0.0 ($SiMe_3$), 18.2 (CH_2–CN), 39.0 (N$CHSi_2$), 48.7 (CH_2–N), 118.9 (*C*N) ppm. IR (cm^{-1}): 3300 (NH), 2200 (CN), 1350 (C–N). MS (EI); *m*/*z*: 228 (12.5), 188 (9.8), 174 (51.5), 155 (52.8), 73 (100).



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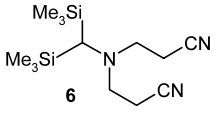
5.4.2. Cyanoethylation of BSMA (1) at reflux

Acrylonitrile (100 ml, stabilized with 35–45 ppm 4-methoxyphenol); glacial acetic acid (1.44 g, 24 mmol) and BSMA (4.2 g, 24 mmol) were introduced in a round-bottomed flask equipped with a magnetic stirring bar and a reflux condenser and the mixture stirred 72 h at reflux. Evaporation of the low boiling materials left a semi-solid residue, which was dissolved in chloroform (40 ml) to separate polyacrylonitrile (filtration on a sintered glass filter) and washed with aqueous ammoniac until neutrality. Drying over magnesium sulfate, filtration and chloroform evaporation left an viscous oil which was dissolved in a chloroform/pentane mixture (10/90) and stored 1 h at −30 °C. Precipitated white solid was recovered under filtration and identified as the dinitrile **6**. Small quantities of mononitrile **5** were found in the filtrate.

5.4.3. N-[Bis(trimethylsilyl)methyl]-3-aminopimelonitrile (6)

M: 281. 47% yield. m.p.: 89 °C. ^{1}H-NMR: δ 0.01 (s, 18H), 1.48 (s, 1H), 2.32 (t, 4H, $^3J = 6.8$), 2.81 (t, 4H, $^3J = 6.9$) ppm. ^{13}C-NMR ($CDCl_3$): δ 1.2 ($SiMe_3$), 18.7 (CH_2–CN), 47.1 (N$CHSi_2$), 52.2 (CH_2–N), 118.8 (*C*N) ppm. IR (cm^{-1}): 2247 (CN), 1250 and 844 ($SiMe_3$). MS (EI); *m*/*z* 281 (6.5), 266 (2.5), 241 (5.8), 208 (100), 98 (33.4), 73 (60).



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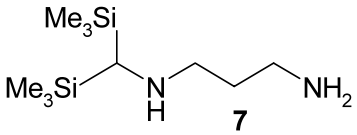
5.5. Reduction of nitrile 5

Freshly distilled diethyl ether (20 ml) was introduced in a three-necked round-bottomed flame-dried flask equipped with a 50 ml dropping funnel, a magnetic stirring bar, a nitrogen inlet and a reflux condenser, and placed in an ice-bath. Under stirring, LAH (0.37 g, 8.8 mmol) was cautiously added. Aminonitrile **5** (2 g, 8.8 mmol) dissolved in ether (10 ml) was slowly added from the funnel and the mixture left 15 h under stirring at room temperature. Reaction flask was placed in ice and, successively, water (0.5 ml), 15% sodium hydroxide (0.5 ml) and water (1.5 ml) were added. Lithium and aluminum salts were separated by filtration on celite. Ether filtrate was washed with water and dried over magnesium sulfate, and ether was evaporated leaving an oil which was purified by distillation.

5.5.1. N-[Bis(trimethylsilyl)methyl]-1,3-diaminopropane (7)

M: 232. 45% yield. b.p.: 68 °C (8 Torr). ^{1}H-NMR: δ −0.09 (s, 18H), 0.98–1.35 (m, 4H, 3H deuterium exchangeable), 1.44 (m, 2H), 2.49 (t, 2H, $^3J = 6.8$), 2.61 (t, 2H, $^3J = 6.7$) ppm. ^{13}C-NMR ($CDCl_3$): δ −0.8 ($SiMe_3$), 34.0 (C–CH_2–C), 39.6 (N$CHSi_2$), 40.5 (CH_2–N), 52.4 (CH_2–N) ppm. MS (EI); *m*/*z*: 232 (0), 217 (3.4), 174 (4.0), 159 (18.7), 116 (100).



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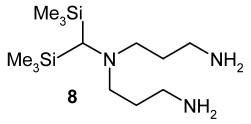
5.6. Reduction of dinitrile 6

Aminodinitrile (2.5 g, 8.89 mmol) dissolved in freshly distilled THF (20 ml) was introduced in a three-necked round-bottomed flame-dried flask (100 ml) equipped with a 100 ml pressure-equalizing dropping funnel, a

magnetic stirring bar, a nitrogen inlet and a reflux condenser connected to a calcium chloride tube, and placed in an ice-bath. Under stirring, a 1 M solution of borane in THF (54 ml, 54 mmol) was slowly added from the funnel and the mixture was kept 12 h at reflux. Reaction flask was cooled with iced water and hydrochloric acid (6 N, 19 ml) was added. After stirring 1.5 h at room temperature, THF was evaporated; reaction mixture was washed with ether (3×20 ml). Aqueous phase was treated with sodium hydroxide pellets until basic and the organic phase, thus liberated extracted with ether (3×20 ml). Etheral solution was dried over magnesium sulfate and ether was evaporated leaving an almost pure yellowish oil.

5.7. 5-[Bis(trimethylsilyl)methyl]-caldine (**8**)

M: 289. 54% yield. ^{1}H-NMR: δ 0.00 (s, 18H), 1.30 (s, 4H, 3H deuterium exchangeable), 1.47 (m, 2H), 1.61 (s, 1H), 2.51 (t, 2H, $^3J = 7.0$), 2.63 (t, 2H, $^3J = 7.0$) ppm. ^{13}C-NMR ($CDCl_3$): δ 1.2 ($SiMe_3$), 34.8 (C–CH_2–C), 39.9 (N$CHSi_2$), 42.5 (CH_2–NH_2), 53.9 (CH_2–N). IR (cm^{-1}): 3353 (NH_2), 1250 and 840 ($SiMe_3$).



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References

[1] J.-P. Picard, Can. J. Chem. 78 (2000) 1363.
[2] Some silicon bioactive compounds: (compound **A**) R. Tacke, U. Wannagat, Topics Curr. Chem. 84 (1979) 1; (compound **A**) E. Lukevics, V.P. Dremova, L.I. Simchenko, M.G. Voronkov, Khimiko-Farmatsevticheskii Zh. 8 (1974) 29 [Chem. Abstr., 82 (1975) 57805]; (compound **A**) E. Lukevics, Biological activity of nitrogen-containing organosilicon compounds, in: Biochemistry of silicon and related problems, Plenum Press, New York, 1978, p. 435; (compound **B**) (compound **C**) Ye.A. Mamayeva, O.V. Agafonova, V.N. Negrebetsky, A.G. Shipov, Yu.I. Baukov, A.S. Losev, Khim. Farm. Zh. 28 (1994) 26 [Chem. Abstr., 122 (1995) 10104]; (compound **D**) S. Barcza, US Patent No. 4132725, 1979 [Chem. Abstr., 90 (1979) 121795]; (compound **E**) W.K. Moberg, US Patent No. 4510136, 1985 [Chem. Abstr., 104 (1986) 207438]; (compound **E**) R. Tacke, B. Becker, D. Schomburg, Appl. Organometal. Chem. 3 (1989) 133; (compound **F**) G.M. Banik, R.B. Silverman, J. Amer. Chem. Soc., 112 (1990) 4499.
[3] Chemistry of vicinal diamines, see for example: D. Lucet, T. Le Gall, C. Mioskowski, Angew. Chem. Int. Ed. 37 (1998) 2580.
[4] Brönsted and Lewis bases, see for example: C.D. Gutsch, G.C. Mei, J. Am. Chem. Soc. 107 (1985) 7964.
[5] Synthesis of heterocycles, see for example: A.E.A Propter, Comprehensive Heterocyclic Chemistry, vol. 3, Pergamon Press, Oxford, 1984, p. 179Synthesis of heterocycles, see for example: .
[6] Polyamines as chiral ligands, see for example: P. Gamez, F. Fache, P. Mangeney, M. Lemaire, Tetrahedron Lett. 34 (1993) 6897.
[7] Polyamines as protecting groups, see for example: (a) A. Alexakis; P. Mangeney, I. Marek, F. Rose-Munch, E. Rose, A. Semra, F. Robert, J. Am. Chem. Soc. 114 (1992) 8288;
(b) A. Alexakis, N. Lensen, P. Mangeney, J. Org. Chem. 57 (1992) 4563.
[8] Polyamines as enantiomeric excess determination auxiliaries, see for example: (a) A. Alexakis, S. Mutti, P. Mangeney, J.F. Normant, Tetrahedron Asymmetry 1 (1990) 437;
(b) A. Alexakis, S. Mutti, J.-C. Frutos, P. Mangeney, J. Org. Chem. 59 (1994) 3326.
[9] See, for instance: (a) V. Quemener, N.A. Khan, J.P. Moulinoux, Cancer J. 3 (1990) 174;
(b) N. Seiler, Digestion 46 (1990) 319.
[10] See web site: http://sunaimed.univ-rennes1.fr/polyamines/strucfr.html.
[11] V.B. Lasev, Zh. Obshch. Khim. 37 (1967) 253 [Chem. Abst. 66 (1967) 95115].
[12] D.J. Peterson, J. Organomet. Chem. 9 (1967) 373.
[13] R. Tacke, Liebigs Ann. Chem. (1980) 1859.
[14] See also: (a) M. Kurono, R. Unno, Y. Matsumoto, Y. Kondo, T. Mitani, T. Jomori, H. Michishita, K. Sawai, Eur. Patent No. 288.002, 1989 [Chem. Abstr., 110 (1989) 75808];
(b) R.D. Haugwitz, W.K. Anderson, R. Kasliwal, D.M. Houston, V.L. Narayanan, Appl. Organomet. Chem. 4 (1990) 375;
(c) W.K. Anderson, R.D. Haugwitz, US Patent No. 4 994 591, 1989 [Chem. Abst. 115 (1991) 92600];
(d) W.K. Anderson, R. Kasliwal, D.M. Houston, Y.-S. Wang, V.L. Narayanan, R.D. Haugwitz, J. Plowman, J. Med. Chem. 38 (1995) 3789.
[15] Concerning the bisimine strategy see, for example: (a) N. de Kimpe, L. D'Hondt, E. Stanoeva, Tetrahedron Lett. 32 (1991) 3879;
(b) M. Svoboda, H. Tom Dieck, C. Krüger, Y.-H. Tsay, Z. Naturforsch. B 36 (1981) 814;
(c) H. Tom Dieck, U. Verfürt, K. Diblitz, J. Ehlers, G. Fendesak, Chem. Ber. 122 (1989) 129.
[16] C. Palomo, J.-M. Aizpurua, J.-M. Garcia, R. Galarza, M. Legido, R. Urchegui, P. Roman, A. Luque, J. Server-Carrio, A. Linden, J. Org. Chem. 62 (1997) 2070.
[17] S. Grelier, T. Constantieux, D. Deffieux, M. Bordeau, J. Dunoguès, J.-P. Picard, Organometallics 13 (1994) 3711.
[18] (a) M.S. Buhlier, W. Wehrner, F. Vögtle, Synthesis (1978) 155.;
(b) R. Moors, F. Vögtle, Chem. Ber. 126 (1993) 2133.
[19] J. Powell, N. James, S.J. Smith, Synthesis (1986) 338.
[20] H.C. Brown, B.C. Subba Rao, J. Am. Chem. Soc. 82 (1960) 681.
[21] (a) J.P. Picard, S. Grelier, J. Dunoguès, J.M. Aizpurua, C. Palomo, J. Organomet. Chem. 419 (1991) C1;
(b) J.P. Picard, S. Grelier, T. Constantieux, J. Dunoguès, J.M. Aizpurua, C. Palomo, M. Petraud, B. Barbe, L. Lunazzi, J.M. Leger, Organometallics 12 (1993) 1378.