Regio- and Diastereoselective Synthesis of α-Cyanoamines by Anodic Oxidation of 6-Membered α-Silylamines

Erwan Le Gall,*[a] Jean-Pierre Hurvois,[a] and Sourisak Sinbandhit[b]

Keywords: C–C coupling / α-Cyanoamines / Electrochemistry / Iminium cation / α-Silylamines

The electrochemical cyanation of *N*-benzyl-substituted cyclic six-membered α-silylamines including tetrahydroquinoline and piperidine derivatives was studied. The results of these investigations demonstrate that α-silylamines are valuable precursors for the preparation of the corresponding α-cyanoamines. The TMS group α to the N atom not only governs the chemoselectivity of the iminium formation through a preferential desilylation reaction under the experimental conditions (i.e., amine cation radical desilylation versus deprotonation), it also lowers the oxidation potential of tertiary amines compared to their non-TMS counterparts. Both the stereoselectivity and regioselectivity of the cyanide addition were investigated with 3-methylpiperidine as the model compound. The formation of a single *cis* diastereoisomer in which the 2-cyano group is axial and the 5-methyl group is equatorial, indicates that the addition of the cyanide anion onto the iminium species is under stereoelectronic control. In addition, the redox reaction involving the intermediate nitrogen-centered cation radical and the cyanide anions played no role, because the α-silyl radical has such a short lifetime.

Introduction

The chemistry of iminium salts is of crucial importance in both the laboratory and in in vivo syntheses of various alkaloids.[1] Most of the initial synthetic attempts towards such intermediate species exploited the enamine → iminium equilibrium to effect additions of electrophiles and nucleophiles, respectively.[2] It is also well reported that such species are stable only under a very restricted set of conditions, and that cyanide anions are useful for trapping iminiums salts. The α-cyanoamines thus obtained have proved to be powerful synthons for the preparation of various piperidine derivatives.[3] Another possibility that has been explored is the direct oxidation of the requisite amine to the desired iminium salt, with oxidizing agents such as mercuric acetate,[4] chlorine dioxide,[5] or dichlorodicyanoquinone[6] to effect the amine → iminium transformation. The product distribution indicated a strong preference for endocyclic oxidation, but unfortunately the behavior of highly unsymmetrical amines such as 3-alkyl-substituted piperidines has not been studied under such reaction conditions, and consequently this more straightforward route has received less attention.

Photochemical or electrochemical methods that are reported to proceed by Single Electron Transfer (SET) have also not received much attention. It is generally performed under milder conditions and the desired α-cyanoamines are obtained in good yields.[7] The general absence of regioselectivity with the electrochemical method limits its utility for the preparation of an otherwise interesting set of intermediates.[8]

Continuing our investigations of the electrochemical preparation of various α-cyanoamines[9] we became interested in the studies of Mariano,[10] who elegantly pointed out the synthetic use of α-silylamines as a valuable source of silylmethylamine cation radicals that can promote intramolecular cyclization. These investigations not only show that the intermediate silylmethylamine cation radical is efficiently desilylated, but also that problems may arise from the use of the incipient α-amino radical intermediate. This latter species is readily oxidized to the corresponding iminium salt, but this unwanted side reaction can be avoided by proper selection of photosensitizer and substituent. In a similar field of research, Fox and Mariano[11] exploited the fact that α-silylamines are easily and regioselectively oxidized to reactive iminium cations which are valuable intermediates in Mannich-type cyclization reactions.

In two recent papers we described the electrochemical cyanation of various aromatic *N*-alkylamines including tetrahydroquinoline, benzazepine, and phenylpiperidine systems.[9] We were able to demonstrate that electrochemistry is an efficient tool for the preparation of the corresponding α-cyanoamines. These efforts also pointed out that problems associated with the nonselective deprotonation at both the $N-CH_2$ positions can be avoided with the right selection of amine *N*-substituents. From our results it also became clear that the regioselectivity of the cyanide addition could be improved. For this, cyclic α-silylamines seemed to be a promising possibility. Our preliminary results on the anodic cyanation of 6-membered cyclic tertiary α-silylamines are presented here.

[a] Laboratoire d'Electrochimie et d'Organométalliques, U.M.R. 6509, Campus de Beaulieu, F-35042 Rennes Cedex, France
Fax: (internat.) + 33-2/99281660
E-mail: jean-pierre.Hurvois@univ-rennes1.fr
[b] Centre Régional de Mesures Physiques de l'Ouest, Campus de Beaulieu, F-35042 Rennes Cedex, France

  1434–193X/99/1010–2645 $ 17.50+.50/0

Results and Discussion

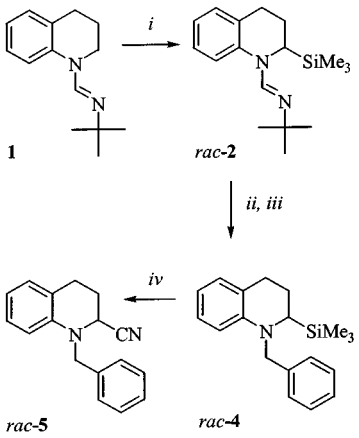
Electrochemical Investigations

A glassy carbon electrode was used for cyclic voltammetry measurements. Peak potentials were expressed in V versus SCE and the ohmic drop was not corrected. The α-silylamine **4** was dissolved in methanol, containing lithium acetate (15 g/l) as supporting electrolyte and sodium cyanide (4 equiv. per mol of substrate) as trapping agent. Under these reaction conditions two irreversible peaks were recorded at +0.5 V and +1.1 V. The first oxidation peak results from the amine → iminium transformation and the second oxidation peak is attributed to the oxidation of α-cyanoamine **5**. In the absence of cyanide anions, a single peak was recorded at +0.5 V. The potential of the first oxidation peak is significantly smaller (Δ = 0.25 V) than that of the non-TMS counterpart (+0.75 V)[9b] whilst the second oxidation peak is unchanged. This result is consistent with that of Cooper,[12] who reported a similar decrease in the first oxidation peak of various aromatic α-silylamines. Yoshida[13] and co-workers also reported a large decrease in the oxidation potential of α-silylcarbamates. On the other hand, each of the voltammograms of the aliphatic α-silylamines **10** and **14**, which were recorded under similar reaction conditions, contained a single peak at +0.75 V.[14] It is worth noting that the cyclic voltammograms of non-TMS counterparts of **10** and **14** in this medium contain no oxidation peaks because of their higher oxidation potential values. Taken together, these results indicate that selective transformations to the desired α-cyanoamines could be performed at the first oxidation peak during macroscale electrolyses.

Oxidation of the Aromatic Silylamine 4

First, we decided to focus our interest on the electrochemical behavior of aromatic α-silylamines. The tetrahydroquinoline system was selected as the model compound and the silylated precursor **4** was prepared according to the method developed by Meyers[15] and co-workers as outlined in Scheme 1. The macroscale electrolysis of **4** was performed at a porous carbon electrode (diameter = 50 mm; thickness = 12 mm). The flow rate of the solution (*f*) percolating through the electrode was regulated at *f* = 5 mL/min and the current was calculated according to Faraday's law for a theoretically 2 Faraday per mol process.

Lithium acetate was selected as the supporting electrolyte and 4 equiv. of sodium cyanide was added in the inlet solution. High conversion yields (up to 95%) were indicated by the disappearance of the first peak in the voltammogram registered at the outlet solution, and therefore no recycling was necessary. Moreover, the second oxidation peak at +1.1 V, attributed to **5**, is evidence of selective transformation at the first oxidation peak. After the usual workup procedure, the crude material was purified by column chromatography to afford the desired cyanoamine **5** as a single product. The ^{1}H-NMR spectra are consistent with ring cyanation and



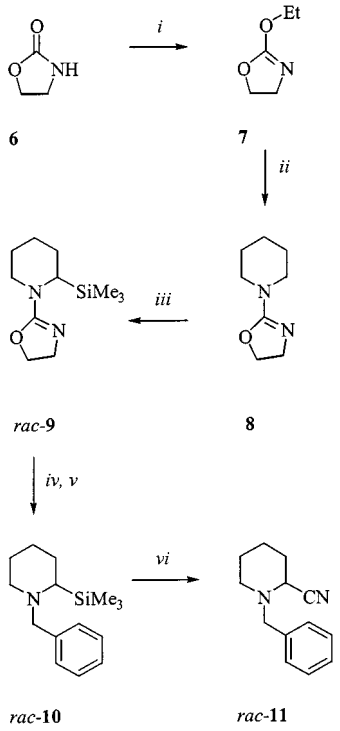
Scheme 1. Reagents and conditions: (*i*) *t*BuLi (1.1 equiv.), THF, −78 °C, Me_3SiCl; (*ii*) N_2H_4, 80 °C, 2 h; (*iii*) BzlBr (1.1 equiv.), aq. Na_2CO_3 (20%), 60 °C, 3 h; (*iv*) − 2 e, − H^+, NaCN (4 equiv.)

contain a characteristic 2-H signal at δ = 4.29. Moreover, the absence of a signal at δ = 0.1 is spectral evidence that the oxidation process yielded an iminium ion at the site of TMS substitution. The high regioselectivity of this sequence prompted us to investigate the piperidine ring system further.

Oxidation of the Aliphatic α-Silylamine 10

The piperidine ring is an integral feature of many natural products.[16] Finding synthetic procedures to functionalize such systems is therefore a significant challenge. In a series of papers, Gawley and co-workers demonstrated that an oxazoline auxiliary mediates the *ortho* metalation of piperidine derivatives.[17] The ethoxyoxazoline **7** was prepared in multigram scale by a two-step procedure starting from the commercially available ethanolamine. Compound **7** was treated with piperidine in the presence of a catalytic amount of NH_4Cl to afford the desired precursor **8**, which may be deprotonated by *s*BuLi in the presence of a catalytic amount of TMEDA (0.1 equiv.). No difficulties were encountered when **10** was synthesized by successive treatments with hydrazine followed by an alkylation with benzyl bromide under classical Schotten−Baumann conditions (Scheme 2). The expected α-silylamine **10** was filtered through a silica column, and it is significant that the α-silylamine can be readily separated from the non-TMS counterpart since they have very different R_f values.

The ^{13}C-NMR spectrum contained a typical doublet signal (^1J = 118 Hz, C-2) at δ = 55 which collapses during a gated decoupling experiment at δ = 1.85 (2-H). The magnitude of the ^3J ax/ax coupling constant (12.0 Hz) indicates that 2-H is in an axial orientation and that the trimethylsilyl group is therefore equatorially situated. Macroscale electrolyses, under the conditions used to oxidize **4**, were carried out on the α-silylamine **10**, which was percolated through the porous anode and electrolyzed. The voltammogram recorded at the outlet solution showed that the oxidation peak disappeared. After electrolysis was completed, the sol-

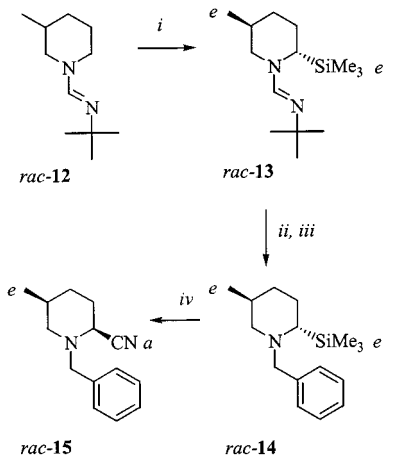


Scheme 2. Reagents and conditions: (*i*) $Et_3O^+BF_4^-$, CH_2Cl_2, 20°C, 16 h; (*ii*) PTSA, 80°C, 5 h; (*iii*) *s*BuLi (1.1 equiv.)/TMEDA (0.1 equiv.), THF, −78°C, Me_3SiCl (1.1 equiv.); (*iv*) N_2H_4, 80°C, 7 h; (*v*) BzlBr (1.1 equiv.), aq. Na_2CO_3 (20%), 60°C, 3 h; (*vi*) − 2 e, − H^+, NaCN (4 equiv.)

vent was distilled off and the crude material was purified by column chromatography to afford **11**[18] as the sole product in 75% yield.

Oxidation of the Unsymmetrical α-Silylamine (14)

Having demonstrated that a piperidine ring can be cyanated in satisfactory yield under these experimental conditions, we decided to apply our method on unsymmetrical amines. To this purpose, the 3-methyl-*N*-benzylpiperidine was selected as the model compound. The electrochemical and chemical preparations of unsymmetrical α-cyanopiperidine derivatives have little preparative value since a mixture of regioisomers is generally obtained.[19] Many synthetic efforts towards such substrates have exploited the presence of a $\Delta^{3,4}$ double bond to control the regiochemistry during the dihydropyridinium salt formation.[20] To overcome the problem associated with the nonselective formation of an iminium salt at the electrode, we took advantage of the fact that unsymmetrical amines could be lithiated regiospecifically.[22] We expected the α-silylamine to be oxidized to a single iminium salt which would lead to the formation of a single α-cyanoamine from the reaction. The synthesis of **14** was therefore performed under the same conditions used to synthesize **4**. The two-step procedure including the lithiation and silylation of **12** afforded **13** as the sole product. The cleavage of the amidine function was carried out under Meyers′ conditions[21] and the alkylation of the intermediate secondary amine with benzyl bromide afforded the desired α-silylamine **14** (Scheme 3). There have been very few literature reports on the two-step lithiation → silylation procedure with unsymmetrical piperidines. However, the stereochemistry of the resulting 2,5-disubstituted amine was assigned to be *trans*.[22a] A detailed examination of the spectrum of **14** confirmed these assignments.



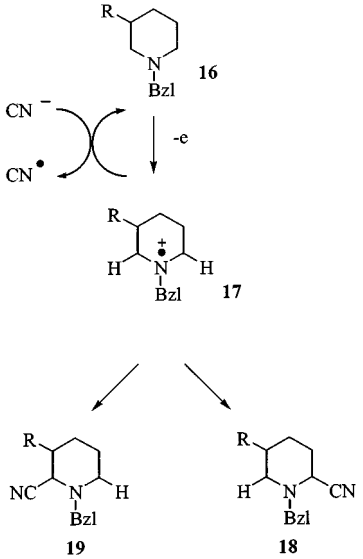
Scheme 3. Reagents and conditions: (*i*) *t*BuLi (1.1 equiv.), THF, −78°C; (*ii*) Me_3SiCl; (*iii*) N_2H_4, 80°C, 7 h; (*iv*) BzlBr (1.1 equiv.), aq. Na_2CO_3 (20%), 60°C, 3 h; (*v*) − 2 e, − H^+, NaCN (4 equiv.)

The large ^3J (6ax/5ax) value for the resonance of 6-H^a at δ = 1.33 clearly indicates that the methyl group (5-CH_3) is equatorial. On the other hand, 2-H gives rise to a doublet of doublets [^3J (2ax/3ax) = 13.65 Hz, ^3J (2ax/3eq) = 2.65 Hz] at δ = 1.74. Taken together these results clearly indicate that both the trimethylsilyl and methyl groups are in a *trans*-diequatorial conformation. The cyanation reaction was readily achieved under the conditions used to oxidize **10**. We were pleased to find that **15** was the only product shown by the ^{1}H-NMR spectrum. On irradition at δ = 1.68 (5-H), the signals at δ = 2.05 (6-H^a) and δ = 0.87 (5-CH_3) collapsed to a doublet and a singlet, respectively, and a vicinal coupling of 5 Hz was also lost from the resonance of 6-H^b. In addition, a broad signal at δ = 3.71 was attributed to 2-H, to place the cyano and the methyl groups in a *cis*-1,4-axial/equatorial orientation.

Mechanism of the Direct Cyanation Procedure

The electrochemical process of tertiary amines has been reviewed by several authors[23] and can be summarized as follows (Scheme 4). The first electron abstraction yields a planar cation radical **17**, a short-lived intermediate, which plays a major role in the oxidative process. The loss of a proton at the N−CH_2 positions is the most fundamental process of such a species, but C−C cleavages[6] have also been encountered instead of deprotonation. If an unsymmetrical starting amine (**16**) is used, the following steps (i.e., deprotonation, oxidation, and subsequent trapping with cyanide anions) lead to a mixture of products, which are cyanated at one of the two ring positions (**18** and **19**), or at the alkyl substituent on the N atom. The product distribution **18**/**19** provides a direct indication of the site of depro-

tonation, but sometimes a single ring-cyanated product (R = H) is detected, a feature long explained by a preferential electrode adsorption mode.[8b] However, structural effects involving the interaction between the partially occupied orbital on the nitrogen atom of the intermediate cation radical and the α-CH orbitals must be taken into account and gives a better explanation for the observed results.[10a,23a,23c,24]

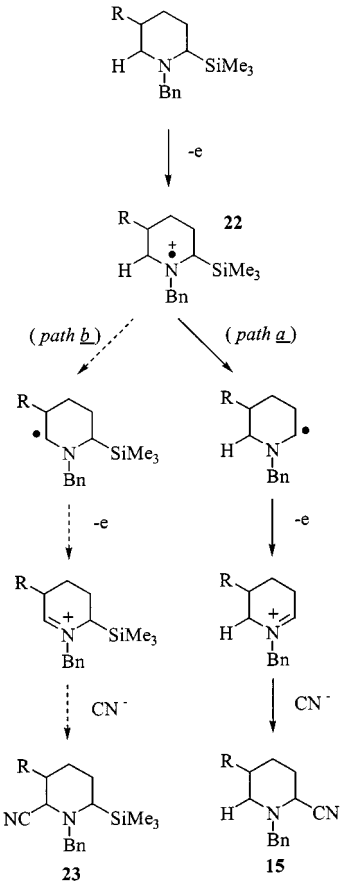


Scheme 4. Electrochemical pathways for the unsymmetrical amine **16** (R = CH_3)

There have been very few publications on the cyanation of 3-alkylpiperidine derivatives, mainly because the oxidation of unsymmetrical amines yield an equimolar mixture of cyano adducts.[19] The nonselective deprotonation reaction (Scheme 4) at either the α or α′ position relative to the nitrogen atom explains the lack of regioselectivity of the cyanide addition.

As confirmation, we carried out the anodic oxidation of the unsymmetrical amine **16** (R = CH_3), and indeed, an unseparable mixture of α-cyanoamines **18** and **19** was detected either by VPC or ^{1}H-NMR spectroscopy. Moreover, the presence of a singlet resonance system at δ = 4.81 is evidence that cyanation has taken place at the *N*-Bzl group.

An examination of our results (Scheme 5) shows that desilylation (path a) of the nitrogen-centered cation radical **22** is a fast process which is responsible for the high yields of the desired α-cyanoamines **5**, **11**, and **15**. It is important to note that cyanide anions play a significant role during the course of the electrochemical reaction. It is well reported that nucleophilic substitution occurs easily at the electropositive silicon atom, and is therefore responsible for the rapid cleavage of the C−Si bond.[25] Our results are in agreement with those reported by Mariano[10] in which it was highlighted that the cleavage of the C−Si bond at the radical cation stage was strongly enhanced by the presence of silophiles like CsF or nBu$_4$NF in MeOH solutions.



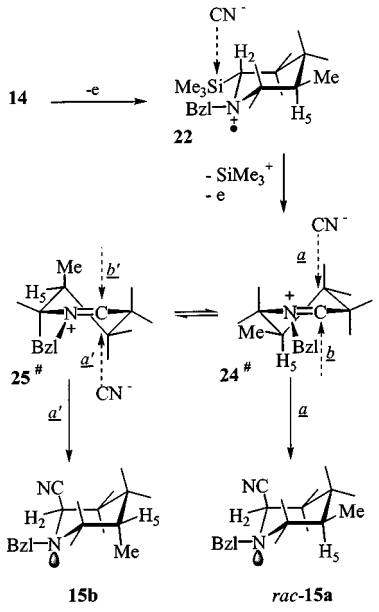
Scheme 5. Electrochemical pathways for the disilylamines **10** (R = H) and **14** (R = CH_3)

The remarkable 2 Faraday per mol process encountered during the macroscale electrolyses performed at a porous graphite felt anode is worthy of additional comment. The current (calculated according to a bielectronic process) is given by the expression i [A] = 2 × f × 96500 × 10^{-3} M/60 (See Experimental Section: General Procedure for the Electrochemical Oxidation). In other words, the current intensity is related to the Faradic process and to the quantity of substance flowing through the porous electrode per second. In our previous studies of the electrochemical preparation of various α-aminonitrile derivatives from aromatic amines, we noticed that under similar reaction conditions coulombic excesses (up to 2 Faraday per mol of substrate) were recorded at the graphite felt anode. For example, it is necessary to raise the quantity of electricity up to 4 Faraday per mol of substrate to transform the *N*-benzylpiperidine to the corresponding cyanoamine in a *single passage* through the porous anode. This points to competitive oxidation which does not consume the substrate but rather the cyanide anions by homogeneous electron transfer[27] involving the transient cation radical species **17** (Scheme 4) and the cyanide anions which are slowly oxidized at the carbon electrode (a 0.5 M methanolic solution of cyanide anions does not give rise to any oxidation peaks under the conditions

used to oxidize the silylamines). Such homogeneous electron transfer was described by Papouchado[26] who reported the oxidation of CN^- to $CN^•$ by the stable radical cation formed by the anodic oxidation of tri-*p*-anisylamine. Generally speaking, the redox reaction involving a substrate and a mediator is under both thermodynamic and kinetic control.[28] However, although the lifetime of the cation radical is often considered to be short, a redox reaction involving the transient intermediate **17** can partially occur in slightly basic media. In contrast, the lifetime of the nitrogen-centered cation radical **22** can be reduced by rapid loss of the $SiMe_3^+$ group (Scheme 5) in the presence of silophiles such as cyanide anions. Therefore, the magnitude of the redox reaction between the TMS-containing cation radical **22** and the cyanide anion will be strongly reduced to that reported for the non-TMS-containing cation radical **17** in which the deprotonation reaction is slow owing to the low acidity of such species.[23a]

Stereoselectivity of the Cyanation Procedure

The important point to note from examination of structures **5**, **11**, and **15,** is that each of them adopts a conformation in which the cyano group is axial. This preferred orientation has been likened by Husson and co-workers to the well-known anomeric effect.[3a] Moreover, the origin of the axial orientation of the cyanide group can be understood if one considers a mechanism with prior formation of an iminium species (Scheme 6). The subsequent approach of the cyanide anion from the axial direction is under stereoelectronic control in which a maximum overlap between the incoming nucleophile and the developing lone pair of the nitrogen atom must be maintained.[29]



Scheme 6. Stereochemical pathway for amine **14**

The addition reaction (path a) between the cyanide anion and the iminium species **24**$^{\#}$, in which the methyl group is equatorial, affords the *cis*-axial/equatorial isomer **15a**. It is also important to note that the alternative isomer **15b**[30] [which result from the axial approach of CN^- to the pseudoaxial methyl isomer **25**$^{\#}$ (path a′)] has never been encountered alongside **15a**.

Molecular mechanics calculations[31] in which the anomeric effect was not considered, showed that the chair conformations of both the *cis* (**15a**) and *trans* isomers (**15b**) are close in energy (i.e., 0.5 kcal/mol). The two iminium species **24**$^{\#}$ and **25**$^{\#}$ are in fact in equilibrium, with an inversion barrier of 0.4 kcal/mol.[32] However, the *trans* system, involving both the iminium compound **25**$^{\#}$ and the α-cyanoamine **15b**, in which the methyl group at C-5 is axial should be higher in energy because of the 1,3-diaxial interaction between the axial hydrogen atom at C-3 and CH_3-5. On the other hand, in the *cis* system (**24**$^{\#}$ and **15a**), a small gauche interaction between the equatorial methyl group and the diequatorial hydrogen atoms 4-H and 6-H is possible, resulting in the energetically more favored conformer **15a**. It should be emphasized that the stereochemical outcome is maintained throughout the course of the cyanation procedure and that the high degree of stereoselectivity encountered is consistent with the hypothesis that an iminium cation is involved in the electrochemical process.

Conclusion

This work is an extension of our previous studies dealing with the electrochemical preparation of various α-cyanoamines. The "electroauxiliary" concept developed by Yoshida and co-workers was applied successfully to the oxidation of either aromatic or aliphatic tertiary amines. Unsymmetrical α-cyanoamines were prepared with complete regio- and stereoselectivity and purification proceeded without difficulties, so that silylated precursors could be prepared in multigram scale. Another interesting property of silanes for synthetic chemists is their stability under rather drastic conditions. This permits a latent functionality which can be liberated when required. In addition, the shift of the oxidation potential of the α-silylamine towards less anodic values allows a selective oxidation without affecting other amino groups which could be present within the structure.

Experimental Section

General: Column chromatography purification was performed with 70−230 mesh silica gel (Merck). − TLC analyses were carried out on alumina sheets precoated with silica gel $60F_{254}$, R_f values are given for guidance. − Elemental analyses were performed at the "Service Central d′Analyse, Département Analyse Elémentaire (Vernaison)." − IR spectra were recorded with a Nicolet 205 FT-IR instrument or a Perkin−Elmer FT-IR 16PC (KBr powder or dichloromethane). − NMR spectra were recorded with a Bruker AH 300 FT spectrometer at the "Centre Régional de Mesures Physiques de l′Ouest (CRMPO)" at 300 MHz (^{1}H) or 75 MHz (^{13}C). Chemical shifts are expressed in ppm downfield from TMS, and coupling constants (J) are given in Hz. The assignments are based on chemical shifts and coupling constants (^1J and long-range coup-

ling). ^{1}H NMR: AB systems are presented in the following order: H^a (δ centered) the more shielded, H^b (δ centered) the more deshielded. ^{13}C NMR: broad-band and gated decoupling spectra were recorded. − High-resolution mass spectra were obtained with a Mat 311 double-focusing instrument at the CRMPO with a source temperature of 170°C. An ion-accelerating potential of 3 kV and ionizing electrons of 70 eV were used. − Analytical capillary gas chromatography was performed with a Hewlett−Packard 5890 gas chromatograph equipped with a programmable temperature control, a flame ionization detector and an HP-5 column (Chrompack CP−Sil 8C, 30 m × 0.32 mm × 0.35 μm).

Materials: All glassware was oven-dried (120°C) over a 24-h period and cooled under a stream of argon. − All reagents were obtained from a commercial source and were distilled prior to use. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone, under N_2. Solutions of *sec*-butyllithium (*s*BuLi) and *tert*-butyllithium (*t*BuLi) were purchase from Acros, used without titration, and stored under argon. Chlorotrimethylsilane (1 M in tetrahydrofuran) was purchased from Aldrich. − Air-sensitive reagents were transferred by syringe or with a double-ended needle. − Triethyloxonium tetrafluoroborate ($Et_3O^+BF_4^-$) was prepared according to ref.[33] The crystalline solid was dissolved in anhydrous CH_2Cl_2 to afford a 2 M solution which was stored at −20°C under N_2 for one month without loss of quality.

General Procedure for the Electrochemical Oxidation: The α-silylamines **4**, **10**, and **14** were dissolved in methanol (Carlo Erba RE 99.6%), containing lithium acetate dihydrate (20 g/l, Aldrich 98%) as the supporting electrolyte and sodium cyanide (4 equiv. per mol of substrate) as the cyanating agent. The solution was filtered through a Millipore (5 μm) system and electrolyzed in a flow cell[34] (Figure 1) fitted with a graphite felt anode (diameter = 50 mm, thickness = 12 mm). The flow rate (*f*) of the solution was regulated by a peristaltic pump at f = 5 mL/min, and the current ($i_1 + i_2$) calculated according to a bielectronic process (2) is given by the expression: i [A] = 2 × f × 96500 × 10^{-3} M/60 where M represents the molar concentration of the substrate. The outlet solution was concentrated under reduced pressure, the crude material was taken up in water (100 mL/g of the starting compound) and extracted with dichloromethane (2 × 100 mL/g of the starting compound). The organic layer was dried with $MgSO_4$ and concentrated. The α-cyanoamines **5**, **11**, and **15** were purified by column chromatography on silica gel (eluent: diethyl ether and petroleum ether).

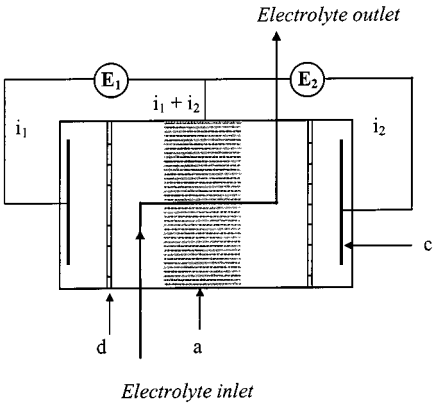


Figure 1. Flow cell design;[34] a: porous anode (graphite felt); c: cathode (stainless steel); d: cationic membranes; E_1, E_2: power supply

1-Benzyltetrahydroquinoline-2-carbonitrile (5)

Synthesis of Amidine 1: To a solution containing the formamide derivative of the tetrahydroquinoline (8.05 g, 50 mmol) in dry CH_2Cl_2 (100 mL) was added dropwise (by double-ended needle) 1.1 equiv. of $Et_3O^+BF_4^-$. The reaction mixture was stirred at room temperature for 16 h under N_2. *tert*-Butylamine (4.38 g, 1.2 equiv. in 10 mL of CH_2Cl_2) was added dropwise over a 30-min period and was allowed to react with the imidate salt at room temperature for an additional 5 h. The solvent was distilled off under reduced pressure and the crude oil was purified by distillation (bp 90−95°C, 1 × 10^{-2} Torr) to afford **1** as a colorless oil (80%); VPC: t_R = 8.0 min (120−220°C at 9°C/min).

***tert*-Butyl(3,4-dihydro-2*H*-quinolin-1-ylmethylene)amine (1):** ^{1}H NMR ($CDCl_3$/200 MHz): δ = 1.25 [s, 9 H, $C(CH_3)_3$], 1.90 (quint, ^3J = 6.0 Hz, 2 H, 3-H), 2.75 (t, ^3J = 6.5 Hz, 2 H, 4-H), 3.75 (t, ^3J = 6.2 Hz, 2 H, 2-H), 6.80−7.20 (m, 4 H), 8.15 (s, 1 H, N=C−H).

Metalation of 1:[15c] To a solution containing the amidine **1** (4.32 g, 20 mmol) in THF (40 mL) at −78°C was added (by syringe) 1.1 equiv. of *t*BuLi. The solution was allowed to warm to −25°C and was stirred for 1 h at −25°C to afford a red anion solution. The solution was cooled to −78°C and Me_3SiCl (1.1 equiv.) was added by syringe and the solution turned slightly yellow. The solution was allowed to warm up to −30°C for 1 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 in the presence of K_2CO_3 (10%). The combined organic phases were dried with $MgSO_4$ and concentrated in vacuo. The crude material was distilled (bp 103°C, 3 × 10^{-2} Torr) to afford **2** as colorless oil (4.9 g, 85%); VPC: t_R = 9.3 min (120−220°C at 9°C/min).

***tert*-Butyl(2-trimethylsilyl-3,4-dihydro-2*H*-quinolin-1-ylmethylene)amine (2):** ^{1}H NMR ($CDCl_3$/200 MHz): δ = 0.00 [s, 9 H, $Si(CH_3)_3$], 1.15 [s, 9 H, $C(CH_3)_3$], 1.80−2.20 (m, 2 H, 3-H), 2.60−2.83 (m, 2 H, 4-H), 4.36 (t, ^3J = 5.7 Hz, 1 H, 2-H), 6.80−7.18 (m, 4 H), 8.03 (s, 1 H, N=C−H).

Hydrazinolysis of 2: The following is adapted from a general procedure described by A. I. Meyers.[15b] To a solution (20 mL, water/ethanol = 1:1) of **2** (0.56 g) was added 3 equiv. (0.5 mL) of glacial AcOH followed by 3 equiv. (0.52 mL) of 98% hydrazine. The reaction mixture was refluxed for 1 h and poured onto a solution of KOH (10%) and extracted with Et_2O. The combined organic layers were dried with K_2CO_3 and concentrated in vacuo. The crude material was purified by column chromatography (diethyl ether/petroleum ether, 10:90) to afford the α-silylamine **3** (0.5 g, 70%) as a colorless oil.

2-Trimethylsilyl-1,2,3,4-tetrahydroquinoline (3): ^{1}H NMR ($CDCl_3$/200 MHz): δ = 0.00 [s, 9 H, $Si(CH_3)_3$], 1.57−1.80 (m, 1 H, 3-H^a), 1.83−2.00 (m, 1 H, 3-H^b), 2.64−2.80 (m, 3 H, 2-H and 4-H), 6.41 (d, ^3J = 8.2 Hz, 1 H, 8-H), 6.53 (t, ^3J = 7.2 Hz, 1 H, 6-H), 6.82−6.99 (m, 2 H, 5-H and 7-H).

Benzylation of 3: The α-silylamine **3** (0.5 g) was refluxed for 2 h in a 10% K_2CO_3 solution in the presence of 1 equiv. of BzlBr. The solution was extracted with Et_2O, dried with K_2CO_3, and concentrated in vacuo. The crude oil was chromatograped on silica gel (diethyl ether/petroleum ether, 10:90) to afford **4** as a slightly yellow oil (0.64 g, 90%).

1-Benzyl-2-trimethylsilyl-1,2,3,4-tetrahydroquinoline (4): ^{1}H NMR ($CDCl_3$/200 MHz): δ = 0.00 [s, 9 H, $Si(CH_3)_3$], 1.90−2.28 (m, 2 H, 3-H), 2.70−2.90 (m, 2 H, 4-H), 3.05 (td, ^3J = 3.6 Hz, ^4J = 1.2 Hz, 1 H, 2-H), 4.35 (AB, ^2J = 16.7 Hz, 1 H, 2′-H^a), 4.69 (AB, ^2J = 16.7 Hz, 1 H, 2′-H^b), 6.40−6.60 (m, 2 H, 6-H and 8-H), 6.83−7.00 (m, 2 H, 5-H and 7-H), 7.13−7.38 (m, 5 H).

Electrolysis of α-Silylamine 4: Compound **4** (0.6 g, 2.1 mmol) was dissolved in methanol (0.5 L) and oxidized (i = 70 mA) in the presence of sodium cyanide (4 equiv.) and lithium acetate. Chromatographic purification (diethyl ether/petroleum ether, 10:90) gave **5**[9b] (0.350 g, 70%).

1-Benzyltetrahydroquinoline-2-carbonitrile (5): ^{1}H NMR ($CDCl_3$): δ = 2.20−2.30 (m, 2 H, 3-H), 2.83 [dt, ^2J(4a,4b) = 16.4 Hz, ^3J(4a,3) = 3.8 Hz, 1 H, 4-H^a], 3.18 [ddd, ^2J(4b,4a) = 16.4 Hz, ^3J(4b,3) = 10.4 Hz, ^3J(4b,3) = 6.9 Hz, 1 H, 4-H^b], 4.29 (m, 1 H, 2-H), 4.34 [AB, ^2J(2′a,2′b) = 16.3 Hz, 1 H, 2′-H^a], 4.77 [AB, ^2J(2′b,2′a) = 16.3 Hz, 1 H, 2′-H^b], 6.68 [d, ^3J(8,7) = 8.4 Hz, 1 H, 8-H], 6.76 [td, ^3J(6,5 and 7) = 7.4 Hz, ^4J(6,8) = 1.0 Hz, 1 H, 6-H], 7.02−7.10 (m, 2 H, 5-H and 7-H), 7.25−7.38 (m, 5 H, 4′-H to 6′-H). − ^{13}C NMR ($CDCl_3$): δ = 24.47 (C-4), 25.55 (C-3), 49.55 (C-2), 53.93 (C-2′), 112.63 (C-8), 118.60 (CN), 118.80 (C-6), 121.72 (C-4a), 126.98 (C-4′), 127.58 (C-7), 127.62 (C-6′), 128.88 (C-5′), 129.25 (C-5), 136.87 (C-3′), 142.77 (C-8a).

1-Benzylpiperidine-2-carbonitrile (11)

Synthesis of Oxazolidin-2-one (6): 61 g (1 mol) of ethanolamine and 13.8 g (0.1 equiv.) of K_2CO_3 were heated (145°C) in the presence of diethyl carbonate (240 g, 2 equiv.) in a three-necked flask. Ethanol was distilled off during 2 h. After cooling, the crude oil was extracted with CH_2Cl_2 (3 × 200 mL) and the resulting solution was filtered through a Buchner funnel. Excess diethyl carbonate and CH_2Cl_2 were distilled off and the solid oxazolidin-2-one was crystallized from ethyl acetate (white plates, mp 86°C, 52 g, 60%).

Oxazolidin-2-one (6): ^{1}H NMR ($CDCl_3$/200 MHz): δ = 3.61 (t, ^3J = 6.8 Hz, 2 H, C=N−CH_2−), 4.42 (t, ^3J = 6.8 Hz, 2 H, O−CH_2−), 6.15 (s, br., 1 H, NH).

Synthesis of Ethoxydihydrooxazole (7): To a solution of oxazolidin-2-one (**6**) (21.75 g, 0.25 mol) in dry CH_2Cl_2 (100 mL) was added (0°C) dropwise (by double-ended needle) a solution containing 1.1 equiv. of $Et_3O^+BF_4^-$. The colorless solution was stirred at room temperature for 16 h. The solution was poured onto a cold saturated sodium carbonate solution. The organic layer was dried with $MgSO_4$ and the solvent was evaporated in vacuo (< 40°C). The crude material was distilled (bp 45°C, 2.5 Torr) from CaH_2 to afford **7** (22.5 g, 80%) as a colorless oil.

2-Ethoxy-4,5-dihydrooxazole (7): ^{1}H NMR ($CDCl_3$/200 MHz): δ = 1.29 (t, ^3J = 7.1 Hz, 3 H, O−CH_2−CH_3), 3.75 (t, ^3J = 8.4 Hz, 2 H, C=N−CH_2−), 4.21 (q, ^3J = 7.1 Hz, 2 H, O−CH_2−CH_3), 4.33 (t, ^3J = 8.4 Hz, 2 H, O−CH_2−).

Condensation of Ethoxydihydrooxazole (7) with Piperidine: Ethoxydihydrooxazole (**7**) (9.2 g, 80 mmol), and piperidine (7.5 g, 1.1 equiv.) were refluxed (5 h) in benzene in the presence of a catalytic amount (0.4 g, 0.1 equiv.) of *p*-toluenesulfonic acid. After cooling, the solution was washed with a saturated $NaHCO_3$ solution and extracted with Et_2O. The resulting organic layers were dried with $MgSO_4$ and concentrated in vacuo. The crude material was distilled (bp 70°C, 3 × 10^{-2} Torr) to yield 10 g (80%) of **8**; VPC: t_R = 3.9 min (120−220°C at 9°C/min).

1-(4,5-Dihydrooxazol-2-yl)-piperidine (8): ^{1}H NMR ($CDCl_3$/200 MHz): δ = 1.40−1.55 (m, 6 H, 3-H and 4-H), 3.20−3.30 (m, 4 H, 2-H), 3.70 (t, ^3J = 8.2 Hz, 2 H, C=N−CH_2−), 4.20 (t, ^3J = 8.2 Hz, 2 H, O−CH_2−).

Metalation and Silylation of 8: A solution (40 mL, Et_2O/THF, 9:1), containing a mixture of **8** (3.08 g, 20 mmol) and TMEDA (0.1 equiv.), was cooled to −78°C. An *s*BuLi solution (23 mL, 1.5 equiv., 1.3 M) was added dropwise (by syringe). The solution was warmed up to −24°C and maintained at this temperature for 2 h. The solution was cooled at −100°C and 30 mL of a 1 M solution of Me_3SiCl was added dropwise. The resulting solution was gently warmed to room temperature over 3 h. The solution was quenched by addition of a 20% solution of K_2CO_3 (20 mL) and extracted with CH_2Cl_2, the organic layers were dried with $MgSO_4$ and concentrated. The crude reaction mixture was distilled in vacuo (bp 80°C, 3 × 10^{-2} Torr) to afford **9** in 70% yield (3.2 g); VPC: t_R = 6.0 min (120−220°C at 9°C/min).

1-(4,5-Dihydrooxazol-2-yl)-2-trimethylsilylpiperidine (9): ^{1}H NMR ($CDCl_3$/200 MHz): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 1.35−1.80 (m, 6 H, 3-H to 5-H), 2.85−3.04 (m, 1 H, 2-H), 3.40−3.59 (m, 1 H, 6-H^a), 3.62−3.86 (m, 3 H, 6-H^b and C=N−CH_2−), 4.09−4.30 (m, 2 H, O−CH_2−).

Hydrazinolysis and Benzylation of 9: To a stirred suspension (10 mL, ethanol/water, 1:1) of **9** (0.94 g, 4.15 mmol) was added 0.8 mL of glacial AcOH and 0.7 mL of 98% hydrazine. The reaction mixture was refluxed for 5 h and the reaction was monitored by VPC. After completion, the solution was washed with a KOH solution (10%) and extracted with Et_2O. The solution was dried with $MgSO_4$ and the solvent evaporated in vacuo to afford the secondary silylamine (0.5 g) in 70% yield; VPC: t_R = 2.77 min (90−220°C at 7°C/min). The crude material was further alkylated without further purifications. To a stirred solution (20 mL) of Na_2CO_3 (10%) was added the secondary α-silylamine (1.2 g) in the presence of 1.30 g of BzlBr (1 equiv.). The suspension was refluxed for 2 h and extracted with Et_2O. The organic layers were dried with $MgSO_4$ and concentrated in vacuo. The crude material was chromatographed through a silica column (petroleum ether/ether, 1:1) to yield **10**, 1.5 g (80%) as a viscous oil; VPC: t_R = 7.65 min (120−220°C at 9°C/min).

1-Benzyl-2-trimethylsilylpiperidine (10): R_f = 0.8 (petroleum ether/diethyl ether, 80:20). − IR (neat): $\tilde{\nu}$ = 2708, 2780, 2928, 3026 cm^{-1}. − ^{1}H NMR ($CDCl_3$): δ = 1.13−1.30 (m, 1 H, 4-H^a), 1.40−1.57 (m, 3 H, 3-H^a, and 5-H), 1.63 [dq, ^2J(3a,3b) = 10.0 Hz, ^3J(4,2) = 3.0 Hz, 1 H, 3-H^b], 1.70−1.81 (m, 2 H, 4-H^b and 6-H^a), 1.86 [dd, ^3J(2,3a) = 12.0 Hz, ^3J(2,3b) = 3.0 Hz, 1 H, 2-H], 2.75 [dt, ^2J(6a,6b) = 11.5 Hz, ^3J(6b,5) = 3.5 Hz, 1 H, 6-H^b], 3.07 [d, ^2J(2′a,2′b), 13.0 Hz, 1 H, 2′-H^a], 4.07 [d, ^2J(2′a,2′b), 13.0 Hz, 1 H, 2′-H^b], 7.19−7.36 (m, 5 H). − ^{13}C NMR ($CDCl_3$): δ = 24.94 (C-3), 26.13 (C-4), 27.35 (C-5), 54.15 (C-6), 55.92 (C-2), 61.65 (C-2′), 126.67 (C-6′), 128.14 (C-5′), 128.68 (C-4′), 140.34 (C-3′). − MS; *m*/*z* (%): 247 (1.10) [M$^+$], 232 (5), 174 (100), 91 (74). − $C_{15}H_{25}NSi$: calcd. 247.1756, found 247.1747 (MS). − $C_{15}H_{25}NSi$ (247): calcd. C 72.81, H 10.18, N 5.66, Si 11.35; found C 73.04, H 10.32, N 5.65, Si 10.40.

Electrolysis of 10: Compound **10** (0.45 g, 1.82 mmol) was dissolved in methanol (0.5 L) and was oxidized (i = 60 mA) in the presence of sodium cyanide (4 equiv.) and lithium acetate. Chromatographic purification gave **11** (0.27 g, 75%) as a pale yellow oil.

1-Benzylpiperidine-2-carbonitrile (11): R_f = 0.4 (petroleum ether/diethyl ether, 80:20). − IR (neat): $\tilde{\nu}$ = 2221, 2252 cm^{-1}(CN). − ^{1}H NMR ($CDCl_3$): δ = 1.49−1.89 (m, 6 H, 3-H, 4-H, and 5-H), 2.42 [td, ^2J(6a,6b) = 11.5 Hz, ^3J(6a, 5a) = 11.5 Hz, ^3J(6a, 5a) = 3.0 Hz, 1 H, 5-H^a], 2.79 [dm, ^2J(6a, 6b) = 13.0 Hz, 1 H, 6-H^b], 3.52 [d, ^2J(2′a, 2′b) = 13.0 Hz, 1 H, 2′H^a], 3.69 [d, ^2J(2′a, 2′b) = 13.0 Hz, 1 H, 2′H^b], 3.72 [t, ^3J(2H, 3H) = 3 Hz, 1 H, 2-H], 7.25−7.35 (m, 5 H). − ^{13}C NMR ($CDCl_3$): δ = 20.47 (C-4), 25.01 (C-5), 28.64 (C-3), 49.71 (C-6), 52.09 (C-2), 60.74 (C-2′), 116.70 (CN), 127.57 (C-6′), 128.52 (C-5′), 129.04 (C-4′), 127.02 (C-3′). MS; *m*/*z* (%): 200 (18) [M$^+$], 173 (23), 109 (67), 91 (100). − $C_{13}H_{16}N_2$: calcd.

200.13134; found 200.1318 (MS). − $C_{13}H_{16}N_2$ (200): calcd. C 77.96, H 8.05, N 13.99; found C 77.13, H 8.17, N 13.73.

1-Benzyl-5-methylpiperidine-2-carbonitrile (15)

Synthesis of the Piperidine Formamidine 12: A solution of 3-methylpiperidine (2.5 g, 25 mmol) in 10 mL of toluene was refluxed (6 h) in the presence of 3.2 g (1 equiv.) of *N*,*N*-dimethyl-*N*′-*tert*-butylformamidine[21a] and a catalytic amount (0.150 g) of NH_4Cl. After cooling, the solution was poured onto 20 mL of 10% K_2CO_3 solution and extracted with Et_2O. The organic phases were dried with $MgSO_4$. The crude oil was purified by distillation to afford **12** (3 g, 66%) as a colorless oil (bp 46°C, 5 × 10^{-2} Torr); VPC: t_R = 5.4 min (90−220°C at 7°C/min).

***tert*-Butyl-(3-methylpiperidin-1-ylmethylene)amine (12):** ^{1}H NMR ($CDCl_3$/200 MHz): δ = 0.80 (d, ^3J = 6.6 Hz, 3 H, CH_3-3), 1.08 [s, 9 H, $C(CH_3)_3$], 1.22−1.80 (m, 6 H, 3-H to 5-H and 6-H^a), 2.28 (dd, ^2J = 12.7 Hz, ^3J = 10.5 Hz, 1 H, 2-H^a), 2.61 (td, ^2J = ^3J = 11.6 Hz, ^3J = 3.3 Hz, 1 H, 6-H^b), 3.57 (dm, ^2J = 12.7 Hz, 1 H, 2-H^b), 7.35 (s, 1 H, N=C−H).

Metalation and Silylation of 12: A solution (40 mL, Et_2O/THF, 8:2) of **12** (3.62 g, 20 mmol) was cooled to −78°C and treated dropwise with a 1.5 M solution of *t*BuLi (15 mL). The solution was allowed to warm to −20°C and was maintained at this temperature for 1 h. It was then cooled to −78°C and treated with Me_3SiCl (22 mL, 1.0 M, 1.1 equiv.) for 4 h after which the reaction mixture was warmed up to 0°C. The reaction mixture was diluted with 37% HCl (10 mL) and washed with Et_2O (50 mL); the resulting organic layer was discarded and NaOH pellets were added to the aqueous phase to turn it basic. The aqueous mixture was extracted with CH_2Cl_2 and dried with $MgSO_4$. The crude product was purified by column chromatography on silica gel (petroleum ether/Et_3N, 90:10) to afford **13** as a colorless oil (4.25 g, 85%); VPC: t_R = 9.2 min (120−220°C at 9°C/min).

***tert*-Butyl[(2*R**,5*R**)-5-methyl-2-trimethylsilylpiperidine-1-ylmethylene)]amine (13):** R_f = 0.8 (petroleum ether/Et_3N, 90:10). − IR (CH_2Cl_2): $\tilde{\nu}$ = 1636 cm^{-1} (C=N). − ^{1}H NMR ($CDCl_3$): δ = 0.09 [s, 9 H, $Si(CH_3)_3$], 0.86 (d, ^3J = 6.6 Hz, 3 H, CH_3-5), 0.99−1.04 (m, 1 H, 4-H^a), 1.14 [s, 9 H, $C(CH_3)_3$], 1.30−1.45 (m, 1 H, 3-H^a), 1.50−1.68 (m, 2 H, 3-H^b and 5-H), 1.79−1.89 (m, 1 H, 4-H^b), 2.31 [dd, ^2J(6a,6b) = 12.8 Hz, ^3J(6a,5) = 10.2 Hz, 1 H, 6-H^a], 2.47 [dd, ^3J(2,3) = 10.5 Hz, ^3J(2,3) = 2.8 Hz, 1 H, 2-H], 4.00 [ddd, ^2J(6b,6a) = 12.8 Hz, ^3J(6b,5) = 4.1 Hz, ^4J(6b,4) = 1.4 Hz 1 H, 6-H^b], 7.39 (s, 1 H, N=C−H). − ^{13}C NMR ($CDCl_3$): δ = 0.00 [$Si(CH_3)_3$], 19.22 (CH_3-5), 26.44 (C-3), 30.11 (C-5), 31.50 [$C(CH_3)_3$], 35.15 (C-4), 50.63 (C-2), 53.03 [$C(CH_3)_3$], 53.76 (C-6), 150.81(C=N). − MS; *m*/*z* (%): 254 (10) [M^+], 239 (6), 197 (12), 98 (100). − $C_{14}H_{30}N_2Si$: calcd. 254.21782, found 254.2175 (MS). − $C_{14}H_{30}N_2Si$ (254): calcd. C 66.07, H 11.88, N 11.01, Si 11.04; found C 66.04, H 11.88, N 11.26, Si 11.35.

Deprotection and Benzylation of 13: A solution (ethanol/water, 2:8) of **13** (2 g, 7.86 mmol) and glacial AcOH (1.6 mL) was treated with 98% hydrazine (1.6 mL). The mixture was refluxed for 5 h and the reaction was monitored by VPC, two successive additions of 98% hydrazine were necessary for the completion of reaction. The solution was cooled and poured onto 10 mL of 10% KOH solution and extracted with Et_2O. The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield the secondary α-silylamine [1.2 g; VPC: t_R = 3.4 min (90−220°C at 7°C/min)]. The crude oil was alkylated in the presence of 1.1 equiv. of BzlBr. After being refluxed for 2 h in a 10% solution of $NaHCO_3$ (20 mL), the suspension was extracted with ether and the combined organic layers were concentrated and purified on silica (petroleum ether/ether, 1:1) to yield **14** (1.2 g, 60%); VPC: t_R = 8.0 min (120−220°C at 9°C/min).

(2*R,5*R**)-1-Benzyl-5-methyl-2-trimethylsilylpiperidine (14):** R_f = 0.80 (petroleum ether/ether, 50:50). − IR (CH_2Cl_2): $\tilde{\nu}$ = 1600, 2948, 3026 cm^{-1}. − ^{1}H NMR ($CDCl_3$/300 MHz): δ = 0.10 [s, 9 H, $Si(CH_3)_3$], 0.69 (d, ^3J = 6.5 Hz, 3 H, CH_3-5), 0.75−1.00 (m, 1 H, 4-H^a), 1.33 [t, ^2J(6a,6b) = ^3J(6a,5) = 10.0 Hz, 1 H, 6-H^a], 1.45−1.68 (m, 3 H, 3-H, and 5-H),1.70−1.79 (m, 2 H, 2-H and 4-H^b), 2.68 [ddd, ^2J(6b,6a) = 11.5 Hz, ^3J(6b,5) = 3.5 Hz, ^4J(6b,4) = 1.5 Hz, 1 H, 6-H^b], 3.0 [d, ^2J(2′a,2′b) = 13.1 Hz, 1 H, 2′-H^a], 4.05 [d, ^2J(2′b,2′a) = 13.1 Hz, 1 H, 2′-H^b], 7.19−7.42 (m, 4 H,). − ^{13}C NMR ($CDCl_3$/75 MHz): δ = −1.22 [$Si(CH_3)_3$], 19.93 (CH_3-5), 27.68 (C-5), 29.98 (C-3), 35.08 (C-4), 55.36 (C-2), 61.58 (C-2′), 62.01 (C-6), 126.67 (C-6′), 128.17 (5′), 128.65 (C-4′), 140.32 (C-3′). − MS; *m*/*z* (%): 261(< 1) [M^+], 188 [M − $SiMe_3$]$^+$ (100), 91 (57). − $C_{16}H_{27}NSi$: calcd. 261.19127; found 261.1911 (MS). − $C_{16}H_{27}NSi$ (261): calcd. C 73.49, H 10.41, N 5.36, Si 10.74; found C 71.41, H 9.75, N 4.88, Si 10.10.

Electrolysis of 14: Compound **14** (0.825 g, 3.15 mmol) was dissolved in methanol (0.5 L) and oxidized (*i* = 101 mA) in the presence of sodium cyanide (4 equiv.) and lithium acetate. Chromatographic purification (diethyl ether/petroleum ether, 50:50) gave **15** (0.55 g, 80%) as a pale yellow oil.

(2*R,5*R**)-1-Benzyl-5-methylpiperidine-2-carbonitrile (15):** R_f = 0.80 (petroleum ether/ether, 50:50). − IR (CH_2Cl_2): $\tilde{\nu}$ = 2220 cm^{-1} (CN). − ^{1}H NMR ($CDCl_3$/300 MHz): δ = 0.88 (d, ^3J = 6.4 Hz, 3 H, 5-CH_3), 1.12−1.35 (m, 1 H, 4-H^a), 1.62−1.91 (m, 4 H, 3-H, 4-H^b and 5-H), 2.05 [t, ^2J(6a,6b) = ^3J(6a,5) = 11.5 Hz, 1 H, 6-H^a], 2.76 [dm, ^2J(6b,6a) = 11.7 Hz, 1 H, 6-H^b], 3.52 [d, ^2J(2′a,2′b) = 13.2 Hz, 1 H, 2′-H^a], 3.68 [d, ^2J(2′b,2′a) = 13.2 Hz, 1 H, 2′-H^b], 3.70 (s, br., 1 H, 2-H), 7.23−7.37 (m, 4 H, H). − ^{13}C NMR ($CDCl_3$/75 MHz): δ = 19.24 (CH_3-5), 28.60 (C-4), 29.04 (C-3), 30.75 (C-5), 51.53 (C-2), 57.07 (C-6), 60.51 (C-2′), 116.61 (CN), 127.60 (C-6′), 128.53 (C-5′), 128.98 (C-4′), 137.01 (C-3′). − MS; *m*/*z* (%): 214 (10) [M^+], 187 (6) [M^+ − HCN], 157 (14), 123 (20), 91 (62), 84 (26), 57 (100), 41 (61), 28 (43). − $C_{14}H_{18}N_2$: calcd. 214.14700, found 214.1480 (MS). − $C_{14}H_{18}N_2$ (214): calcd. C 78.46, H 8.47, N 13.07; found C 78.84, H 8.56, N 12.58.

Acknowledgments

The authors would like to thank Dr. R. E. Gawley for information on the preparation of the Meerwein salt and the oxazolidinone (**7**).

[1] D. J. Hart, in *Alkaloids* (Ed.: S. W. Pelletier), Wiley Interscience, New York, **1988**, vol. 6, p. 228−296.
[2] [2a] E. Wenkert, C. J. Chang, H. P. S. Chawla, D. W. Cochran, E. W. Hagaman, J. C. King, K. Orito, *J. Am. Chem. Soc*. **1976**, *98*, 3645−3655. − [2b] C. Heathcock, M. H. Norman, D. A. Dickman, *J. Org. Chem*. **1990**, *55*, 798−811. − [2c] M. H. Norman, C. H. Heathcock, *J. Org. Chem*. **1988**, *53*, 3370−3371. − [2d] R. V. Stevens, *Acc. Chem. Res*. **1977**, *10*, 193−198.
[3] [3a] M. Bonin, J. R. Romero, D. S. Grierson, H. P. Husson, *J. Org. Chem*. **1984**, *49*, 2392−2400. − [3b] D. S. Grierson, J. L. Bettiol, I. Buck, H. P. Husson, *J. Org. Chem*. **1992**, *57*, 6414−6421. − [3c] D. S. Grierson, J. Royer, L. Guerrier, H. P. Husson, *J. Org. Chem*. **1986**, *51*, 4475−4477. − [3d] Z. Zhu, J. C. Quirion, H. P. Husson, *Tetrahedron Lett*. **1989**, *30*, 5137−5140. − [3e] D. S. Grierson, M. Harris, H. P. Husson, *J. Am. Chem. Soc*. **1980**, *102*, 1064−1082.
[4] [4a] F. Compernolle, M. A. Saleh, S. Toppet, G. Hoornaert, *J. Org. Chem*. **1991**, *56*, 5192−5196. − [4b] S. Van den Branden, F. Compernolle, G. Hoornaert, *Tetrahedron* **1992**, *48*, 9753−9766. − [4c] F. Compernolle, M. A. Saleh, S. Van den

Branden, S. Toppet, G. Hoornaert, *J. Org. Chem.* **1991**, *56*, 2386−2390.
[5] C. K. Chen, A. G. Hortman, H. R. Marzabati, *J. Am. Chem. Soc*. **1988**, *110*, 4829−4831.
[6] R. J. Sundberg, P. J. Hunt, P. Desos, K. G. Gadamasetti, *J. Org. Chem*. **1991**, *56*, 1689−1692.
[7] [7a] J. Santamaria, M. T. Kaddachi, *Synlett* **1991**, 739−740. − [7b] J. Santamaria, M. T. Kaddachi, C. Ferroud, *Tetrahedron Lett*. **1992**, *33*, 781−784. − [7c] J. Santamaria, M. T. Kaddachi, J. Rigaudy, *Tetrahedron Lett*. **1990**, *31*, 4735−4738.
[8] [8a] S. Andreades, E. W. Zahnov, *J. Am. Chem. Soc*. **1969**, *91*, 4181−4190. − [8b] T. Chiba, Y. Takata, *J. Org. Chem*. **1977**, *42*, 2973−2977.
[9] [9a] S. Michel, E. Le Gall, J. P. Hurvois, C. Moinet, A. Tallec, P. Uriac, L. Toupet, *Liebigs Ann.* **1997**, 259−267. − [9b] E. Le Gall, J. P. Hurvois, T. Renaud, C. Moinet, A. Tallec, P. Uriac, S. Sinbandhit, L. Toupet, *Liebigs Ann*. **1997**, 2089−2101. − [9c] E. Le Gall, T. Renaud, J. P. Hurvois, A. Tallec, C. Moinet, *Synlett* **1998**, 513−515.
[10] [10a] W. Xu, P. S. Mariano, *J. Am. Chem. Soc*. **1991**, *113*, 1431−1432. − [10b] W. Xu, Y. T. Jeon, E. Hasegawa, U. C. Yoon, P. S. Mariano, *J. Am. Chem. Soc*. **1989**, *111*, 406−408. − [10c] E. Hasegawa, W. Xu, P. S. Mariano, U. C. Yoon, J. U. Kim, *J. Am. Chem. Soc*. **1988**, *110*, 8099−8111.
[11] X. Zhang, Y. S. Jung, P. S. Mariano, M. A. Fox, P. S. Martin, J. Merkert, *Tetrahedron Lett*. **1993**, *34*, 5239−5242.
[12] B. E. Cooper, W. J. Owen, *J. Organomet. Chem*. **1971**, *29*, 33−40.
[13] [13a] J. I. Yoshida, S. Isoe, *Tetrahedron Lett.* **1987**, *28*, 6621−6624. − [13b] J. I. Yoshida, T. Murata, S. Isoe, *J. Organomet. Chem.* **1988**, C23−C27.
[14] Acyclic α-silylamines[11] have similar oxidation values (+0.68 V versus SCE) but the measurements were performed at a carbon electrode in MeCN in the presence of nBu$_4$NPF$_6$ as supporting electrolyte.
[15] [15a] A. I. Meyers, S. Hellring, *Tetrahedron Lett*. **1981**, *22*, 5119−5122. − [15b] A. I. Meyers, L. M. Fuentes, Y. Kubota, *Tetrahedron* **1984**, *40*, 1361−1370. − [15c] A. I. Meyers, G. Milot, *J. Org. Chem*. **1993**, *58*, 6538−6540.
[16] J. Leonard, in *The Chemistry of Natural Products* (Ed.: R. H. Thomson), Blackie Academic, London, **1993**, p. 218−258.
[17] [17a] K. Rein, M. Goicoechea-Papas, T. V. Anklekar, G. C. Hart, G. A. Smith, R. E. Gawley, *J. Am. Chem. Soc.* **1989**, *111*, 2211−2217. − [17b] R. E. Gawley, G. C. Hart, L. J. Bartolotti, *J. Org*. *Chem*. **1989**, *54*, 175−181. − [17c] R. E. Gawley, Q. Zhang, *J. Org. Chem*. **1995**, *60*, 5763−5769.
[18] Compound **11** was previously described and our ^{13}C-NMR data are indentical to those reported in ref.[3a]
[19] [19a] R. Jokela, T. Tamminen, M. Lounasmaa, *Heterocycles* **1985**, *23*, 1707−1722. − [19b] R. Jokela, M. Lounasmaa, *Tetrahedron* **1987**, *43*, 6001−6006. − [19c] R. Jokela, E. Karvinen, A. Tolvanen, M. Lounasmaa, *Tetrahedron* **1988**, *44*, 2367−2375.
[20] [20a] M. Lounasmaa, J. Miettinen, P. Hanhinen, R. Jokela, *Tetrahedron Lett*. **1997**, *38*, 1455−1458. − [20b] M. Lounasmaa, E. Karvinen, A. Koskinen, R. Jokela, *Tetrahedron* **1987**, *43*, 2135−2143. − [20c] For an overview of the chemistry of the 2-cyano-Δ^3-piperidine system, see: H. P. Husson, J. Royer, *Adv. Use Synthons Org. Chem.* **1995**, *2*, 4−23.
[21] [21a] A. I. Meyers, P. D. Edwards, W. F Riecker, T. R. Bailey, *J. Am. Chem. Soc.* **1984**, *106*, 3270−3276. − [21b] A. I. Meyers, P. D. Edwards, T. R. Bailey, G. E. Jagdman, *J. Org. Chem*. **1985**, *50*, 1019−1026.
[22] [22a] P. Beak, W. K. Lee, *J. Org. Chem*. **1993**, *58*, 1109−1117. − [22b] P. Beak, W. J. Zajdel, D. B. Reitz, *Chem. Rev.* **1984**, *84*, 471−523.
[23] [23a] Y. L. Chow, W. C. Danen, S. F. Nelsen, D. H. Rosenblat, *Chem. Rev.* **1978**, *78*, 243−274. − [23b] E. Steckan in *Organic Electrochemistry*, 3rd ed. (Eds.: H. Lund, M. M. Baizer), Dekker, New York, **1991**, p. 583. − [23c] F. D. Lewis, T-I. Ho, J. T. Simpson, *J. Org. Chem*. **1981**, *46*,1077−1082.
[24] S. F. Nelsen, J. T. Ippoliti *J. Am. Chem. Soc*. **1986**, *108*, 4879−4881.
[25] P. D. Magnus, T. Sarkar, S. Djuric in *Comprehensive Organometallic Chemistry* (Ed.: G. Wilkinson), Pergamon Press, Oxford, **1982**, vol. 7, p. 515.
[26] L. Papouchado, R. N. Adams, S. W. Feldberg, *J. Electroanal. Chem*. **1969**, *21*, 408−410.
[27] See, for example: E. Steckan in *Organic Electrochemistry*, 3rd ed. (Eds.: H. Lund, M. M. Baizer), Dekker, New York, **1991**, p. 593.
[28] C. P. Andrieux, C. Blocman, J. M. Dumas-Bouchiat, F. M′Halla, J. M. Saveant, *J. Am. Chem. Soc.* **1980**, *102*, 3806−3813.
[29] [29a] For a discussion of the synthetic aspects of stereoelectronic control, see: P. Deslongchamps in *Stereoelectronic Effects in Organic Chemistry* (Ed.: J. Baldwin), Pergamon Press, Oxford, **1983**, p. 209. − [29b] R. V. Stevens, *Acc. Chem. Res.* **1984**, *17*, 289−296. For the sake of clarity pathways *b* and *b′* were not considered. However, attack from the lower axial direction (*b*) leads to an unfavorable boatlike transition intermediate whereas that from the upper face (*a*) yields an energetically more favored chairlike transition state.
[30] Compound **15b** was previously synthesized in 15% yield (A. Padwa, W. Dent, H. Nimmesgern, M. K. Venkatramanan, G. S. K. Wong, *Chem. Ber*. **1986**, 813−828). A doublet resonance system (δ = 0.89, J = 6.50 Hz, CH$_3$-5) appears in the ^{1}H-NMR spectrum and the stereochemistry of the 2,5-disubstituted amine was assigned *trans* on the basis of mechanistic considerations.
[31] The calculations were performed with a Silicon Graphics station using the program SYBYL version 6.4.
[32] For a discussion, see: E. Eliel in *Stereochemistry of Organic Compounds*, Wiley, New York, **1994**, p. 665−834.
[33] H. Meerwein in *Org. Synth., Coll. Vol.* **1973**, *5*, 1080−1082.
[34] C. Moinet, E. Raoult, *Bull. Soc. Chim. Fr.* **1991**, 214−221.

Received March 25, 1999
[O99185]