An Organosilicon Route to the B-Norbenzomorphan Skeleton

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Organosilicon compounds are receiving increased attention on account of their interesting chemical properties, which have resulted in synthetic applications.[1] Organosilicon chemistry has therefore become important in the methodology of organic synthesis. Despite evident potential applications of benzofused six- and seven-membered heterocycles in medicinal chemistry,[2] only limited results are available on the silylation of heterocyclic compounds. Of particular interest in this regard is the case of quinoline derivatives that could lead to new organosilicon synthon development.

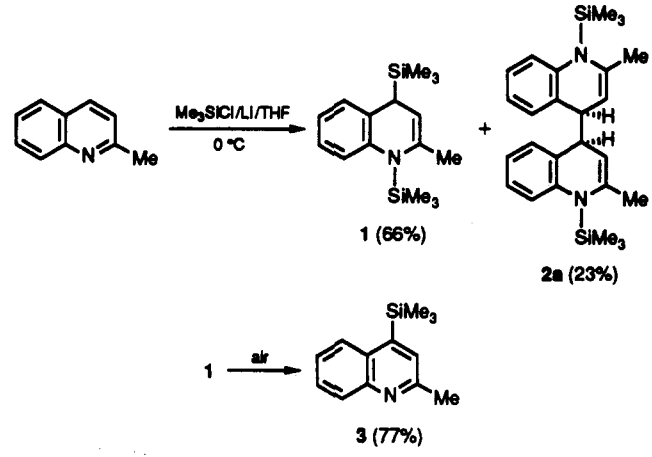
The only literature in this area concerns the silylation of quinoline itself.[3,4] We previously showed[4] that it is possible to increase yields of silylated products and modify the course of the reaction by varying the experimental conditions. We report now results on quinaldine using two silylation reagents: $Me_3SiCl/Li/THF$ and $Me_3SiCl/Mg/THF$. The influence of the metal upon the regio- and stereochemistry of silylation is probed; the chemical behavior of the N-silylated products is investigated and interpreted by quantum mechanics calculations.

Results and Discussion

Treating quinaldine with lithium (2 equiv) and trimethylchlorosilane (2.6 equiv) in THF gave a mixture of two N-silylated products resulting from the reductive silylation of the nitrogenous ring (Scheme I). The reaction went to completion in 5 h at 0 °C; 1,4-bis(trimethylsilyl)-1,4-dihydroquinaldine (1) and *N,N'*-bis(trimethylsilyl)-1,1',4,4'-tetrahydro-4,4'-biquinaldine (**2a**) were isolated in yields of 66 and 23%, respectively. The crystal structure of **2a** shows it to be the (*R,S*) isomer (Figure 1, in supplementary material) resulting from the 4,4' coupling of two dihydroquinaldine moieties.

In order to determine the influence of experimental conditions upon the **1**/**2a** ratio, we carried out a number of experiments where temperature, stoichiometry, and the order of reagent introduction were examined (see Experimental Section). They showed that none of these

Scheme I



parameters is a crucial factor in determining the course of silylation. In particular, performing the reaction with only 1 equiv of lithium instead of the two necessary for the formation of **1** could be expected to favor dimerization. In fact, the **1**/**2a** ratio did decrease but the overall yield showed that the disilylation process leading to **1** is always the most important. This conclusion is in agreement with experiments in which Me_3SiCl was added to the mixture of the other reagents (instead of adding the quinaldine), maintaining a low concentration of the silylation agent. Despite this, the disilylation yield always remained close to 60%. It is worth noting that a large excess of reagent (6 equiv) never led to tetra- or hexasilylated products as obtained from quinoline.[4] Compound **1**, when exposed to air aromatized, yielding 4-(trimethylsilyl)quinaldine (**3**), which is an usual reaction of *N*-silyldihydroquinolines.[5] The structure of compound **3** was confirmed by comparison with the product we previously obtained by selective silylation of the C–Cl bond in 4-chloroquinaldine.[6] Compounds **1** and **2a** were not previously described.

Silylation of quinaldine at 65 °C with magnesium instead of lithium went to completion in 3 h and led to a completely different reaction mixture: ^1H NMR analysis shows three singlets at 0.22, –0.06, and –0.46 ppm with an integration ratio 4/1/1 that is consistent with a 80:20 mixture of dimer and disilyl derivatives. Moreover, we observed no signal at 2.7 ppm as for **1**, but a singlet at 1.3 (3 H) in agreement with a CH_3 group borne by an sp^3 carbon atom linked to a $SiMe_3$ group. However, a rapid evolution in the spectrum was observed regardless of the solvent employed. The low stability of these silylation products, therefore, prevented a more careful structural study. Attempts to isolate pure samples of these products were also unsuccessful. Their chemical behavior compared to those of compounds **1** and **2a** and unambiguous structural proofs of their reaction products, and the fact that reductive silylation of aromatic compounds proceeds through a 1,2- or 1,4- but never a 1,3-addition mechanism,[7] led us to postulate that this mixture consisted of 1,2-bis(trimethylsilyl)-1,2-dihydroquinaldine (**4**) and the *N*-silyl dimer **2b** (Scheme II). Attempts to transform **2b** and **4** into *N*-acetyl derivatives as previously described in the case of quinoline[4] did not succeed: treatment of the reaction mixture with

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(1) For reviews, see: Weber, W. P. *Silicon Reagents for Organic Synthesis*; Springer-Verlag: Berlin, 1983. Colvin, E. W. *Silicon in Organic Synthesis*; Butterworths: London, 1981.
(2) Lednicer, D.; Mitscher, L. A. *The organic chemistry of drug synthesis*; John Wiley and Sons, 1977, Vol. 1, p 337; 1980, Vol. 2, p 362; 1984, Vol. 3, p 183.
(3) (a) Becker, H. P.; Neumann, W. P. *J. Organomet. Chem.* **1972**, *37*, 57. (b) Sulzbach, R. A.; Iqbal, A. F. M. U.S. Pat. 3 781 291 (25 Dec 1973). (c) Nogaideli, A. I.; Akhobadze, D. Ch. *Bull. Acad. Sc. Georgian SSR* **1977**, *87*, 621.
(4) Grignon-Dubois, M.; Fialeix, M.; Rezzonico, B. *Can. J. Chem.* **1990**, *68*, 2153.
(5) Sulzbach, R. A. *J. Organomet. Chem.* **1970**, *24*, 307.
(6) Grignon-Dubois, M.; Fialeix, M. *Bull. Soc. Pharm. Bordeaux* **1988**, *127*, 29; *Chem. Abstr.* **1990**, 112, 179084.
(7) Calas, R. *J. Organomet. Chem.* **1980**, *200*, 11.

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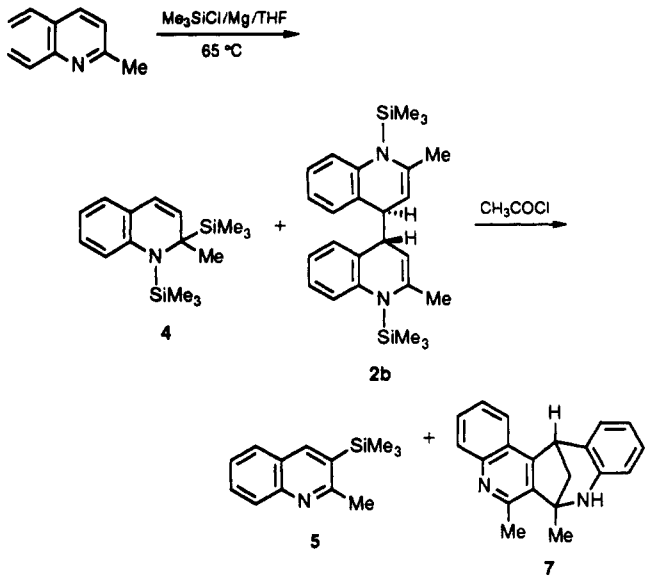
Scheme II



acetyl chloride led only to compounds **5** (18%) and **7** (40%) in addition to intractable tars. The structural attribution of **5** is based on NMR data, especially the ^{13}C chemical shifts that we compared with those of **3**, and calculated values for the 4-(trimethylsilyl)quinaldine and 2-(trimethylsilyl)-3-methylquinoline based on the literature[8] (Table I). Steric hindrance introduced by the silicon group in position 2 could explain the fact that aromatization instead of acylation took place so easily. Attempts to isolate **4** by distillation also led to its aromatization and partial degradation.

Treatment of the mixture of **4** and **2b** with methanol led to the immediate precipitation of a pale yellow solid (mp 135 °C) identified as the quinobenzazepine **6b** (yield: 76% based on quinaldine). We suggest that **6b** resulted from dimer **2b** by a concerted electron transfer as shown in Scheme III. Methanolysis of the remaining N–Si bond in the resulting pentacyclic derivative led to the formation of the NH group. However, taking into account the formation of 1,4-dihydropyridine starting from 1-(trimethylsilyl)-1,4-dihydropyridine and methanol,[9] we cannot exclude the possibility of 1,1′,4,4′-tetrahydrobiquinaldine formation prior to cyclization. On exposure to air at room temperature, **6b** slowly evolved into **7**. Complete transformation under these conditions required 3 to 4 weeks, but only 24 h when dissolved in methanol. It also reacted in chloroform, but more slowly.

In contrast, the meso dimer **2a** when treated with methanol was unchanged after 5 h; its low solubility in this solvent could partially explain this stability. After 24 h, ^1H NMR analysis showed the presence of a small amount of cyclization product **7** in addition to another product (15% yield) identified as 4,4′-biquinaldine (**8**) by comparison with the literature[10] (Scheme IV). Addition of 1 equiv of HMPT allowed complete dissolution of the meso dimer but reaction was quantitative only after 40 h. The intermediate **6a** was not isolated, since the aromatization leading to **7** was too fast. We submited **7** to an X-ray crystallographic study. This allowed unambiguous identification of our compound and therefore confirmed the frame of its precursors **6a** and **6b**. Figure 2 (supplementary material) is a perspective drawing of the molecule with atom labels (hydrogen atoms are omitted for clarity). The fact that both **2a** and **2b** led to the same cyclization product confirms that they are stereoisomers and allows us to attribute the threo linkage to **2b**.

The two pentacyclic products **6b** and **7** were previously reported by Jones et al.[11a] as arising from the treatment of quinaldine with lithium. Their process required 70 to 95 h and led to **6b** in 76–96% yield, but by heating **6b** at 140 °C, **7** was obtained in only 8% yield in addition to another product similar to **9** (16% yield), which we never obtained, and quinaldine (40% yield). These observations are surprising when compared to our results. However, it appears from Jones' paper that the yield for compound **6b** was given before crystallization which he reports to be difficult. The final melting point (mp 135 °C) is in accordance with ours, but that of the crude product (mp 120 °C) is identical to that reported by Levchenko[11b] for an isomer of **6b** for which no formula was proposed. We first thought that the discrepancies observed could be related to a different geometry of compound **6b**. The two possible isomeric forms **6a** and **6b**, which only differ by the stereochemistry around the 4,4′ linkage (Figure 3) were built with Macromodel[12a] (Version 3.0; MM2 forcefield 1987 parameters) and the $^3J(^1H,^1H)$ coupling constants were measured according to the work of Altona et al.[12b] as implemented in the program. These results show that the 0 Hz value reported both by Jones and us for the coupling between H-4 and H-4′ is only compatible with the **6b** isomer (calcd values: 0.7 Hz for **6b** and 6 Hz for **6a**). All these facts, associated with the very low yield of the Jones' aromatization step, could indicate that the crude product obtained by these authors contains only a low concentration of compound **6b**, which could be a less soluble one. Repeating Jones' experiment (96 h reaction time), we effectively obtained **6b** in the first crop, but in only 3% yield. A ^{13}C NMR analysis of the crude product showed the mixture to be very complex. As described by Jones, we treated the crude product with cyclohexane. From the liquid, we isolated an unstable compound whose ^1H NMR spectra is compatible with 1,1′,4,4′-tetrahydro-4,4′-biquinaldine, but the low stability of this dimer did not allow the high field NMR study necessary for a stereochemistry assignment. It slowly evolved quantitatively to **7** (21% yield). The presence of 1,1′,4,4′-tetrahydro-4,4′-biquinaldine in the Jones' sample could explain the reported formation of **9** on heating. However, no NMR data supported the structure attribution for **9**. The cyclohexane insoluble oil was chromatographed on silica gel leading to **10** (5% yield), **11** (4% yield), and quinaldine (32% yield) (Scheme V). Compound **10** obviously resulted from the reaction of THF with a 4-lithio intermediate. When the reaction was stopped after only 24 h, we isolated **12** (10% yield) along with **7** (18% yield) and unreacted quinaldine (50%). Obtention of compounds **10–12** is likely to be a consequence of the low reactivity of quinaldine or its lithio intermediates.

It appears from these results that Me_3SiCl, by trapping the radical-anion intermediate, allowed the dimerization to be considerably faster and regiospecific. The fragility of the Si–N bond with respect to methanol constitutes the driving force of the cyclization step. The two cyclization

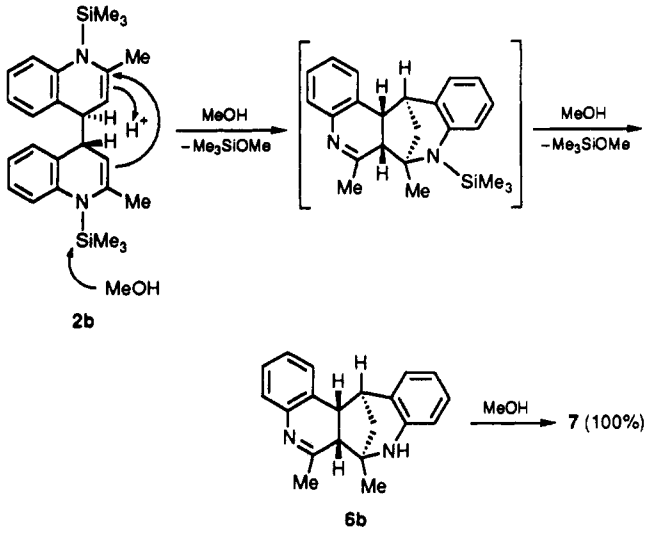
(8) Ewing, D. F. *Org. Magn. Reson.* **1979**, *12*, 499.
(9) Cook, N. C.; Lyons, J. E. *J. Am. Chem. Soc.* **1965**, *87*, 3283.
(10) Yananaka, H.; An-Naka, M.; Kondo, Y.; Sakamoto, T. *Chem. Pharm. Bull.* **1985**, *33*, 4309.
(11) (a) Jones, A. M.; Russel, C. A. *J. Chem. Soc. C* **1971**, 2453. (b) Levchenko, V. V. *Zh. Obschel Khim.* **1948**, *18*, 1245.
(12) (a) Macromodel, developed and distributed by Clark Still, Columbia University, New York. (b) Haasnoot, C. A. G.; De Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

Table I. Calculated and Observed ^{13}C Chemical Shifts for (Trimethylsilyl)quinaldine Isomers[a]

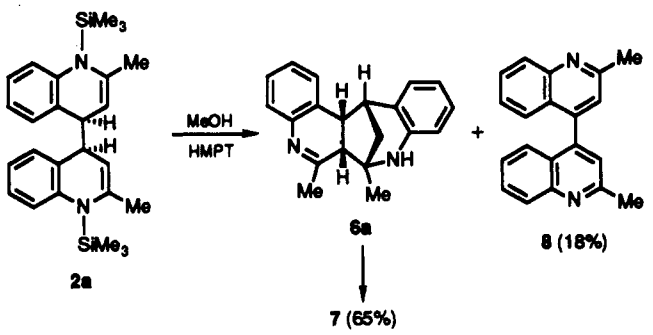
		δ, ppm								
		C_2	C_3	C_4	C_5	C_6	C_7	C_8	C_{4a}	C_{8a}
3	obsd	157.2	125.1	147.0	128.7	127.3	129.6	128.8	129.5	148.3
	calcd	159.5	126.5	148.4	128.5	127.0	129.9	130.5	130.8	149.3
5	obsd	162.7	132.1	143.4	127.4	126.0	128.0	129.7	125.5	147.6
	calcd	165.1	133.2	141.7	128.5	127.0	129.9	130.5	125.2	150.4
4-(trimethylsilyl)quinaldine	calcd	150.1	135.7	147.6	128.5	127.0	129.9	130.5	134.5	145.6
2-(trimethylsilyl)-3-methylquinoline	calcd	164.2	135.4	134.9	128.5	127.0	129.9	130.5	128.5	145.2

[a] 62.86 MHz, $CDCl_3$ used as solvent and internal standard at 77.0 ppm.

Scheme III



Scheme IV



products **6b** and **7** are related to the B-norbenzomorphan skeleton which contains an interesting structural feature for analgesic activity[13] showing the synthetic interest of this process. In order to interpret the difference in the behavior of dimers **2a** and **2b**, they were submitted to a conformational study.

Conformational Studies of Dimers 2a and 2b. The tool of choice for this purpose would have been molecular mechanics using the MM2 force field of Allinger.[14] Unfortunately, the N–Si bond was not parametrized even in the 1987 parameters version, and we turned toward a semiempirical method. We therefore used the MOPAC version 6.0 program[15] implemented in the CHEM-X software package (see Experimental Section for details), which is well adapted to this kind of molecule considering the large number of orbitals involved. Within this program, we chose the MNDO Hamiltonian[16] on account of the parametrized atoms. Starting from the X-ray structure file of dimer **2a**, the C-4–C-4′ bond junction was then rotated by 30° steps and the "cyclization" distance D (C-2···C-3′ or C-3···C-2′) was checked. The conformers giving the shortest distances were selected for full optimization. For stereoisomer **2b**, the chirality of one of the asymmetric carbons in **2a** was inverted and the same procedure as above was then applied. Initially, before optimization, in isomer **2a**, the distances were shorter than in isomer **2b**: from 2.96 to 3.12 Å with a H–C-4–C-4′–H torsion angle between 0° and 60° opposed to 3.86 to 4.01 Å with a H–C-4–C-4′–H angle between 60° and 120°. However, it is worth noting that in the selected conformers of **2a**, the structure is so overcrowded that it was necessary to override the geometry checks of the program by using the keyword GEO-OK showing that **2a** cannot really exist in this geometry. After full optimization, this was confirmed by calculations which gave the following results (converted to kcal/mol): dimer **2a**, lowest energy conformer H–C-4–C-4′–H = 180°, D = 4.61 Å, the "best cyclization" conformer H–C-4–C-4′–H = 60.6°, D = 3.86 Å; dimer **2b**, lowest energy conformer H–C-4–C-4′–H = 60.0°, D = 4.01 Å, the "best cyclization" conformer H–C-4–C-4′–H = 89.97°, D = 3.86 Å.

The "cyclization" distances D are the same in the two isomers but the required conformation is highly disfavored (ΔD = 0.75 Å; ΔE = 6.03 kcal/mol) for isomer **2a** and very near the global minimum for isomer **2b** (ΔD = 0.15 Å; ΔE = 0.30 kcal/mol). In fact, the global minimum for **2a** is found in the X-ray conformation which is very poor for cyclization and the global minimum in **2b** is almost the best conformation for cyclization. This phenomenon is depicted in Figure 3, which shows the cyclization conformation of the two dimers in a Newman projection along the C-4–C-4′ bond: the steric hindrance introduced by the silyl groups in **2a** is highly unfavorable to the cyclization process. On the other hand, isomer **2a** was found to be the thermodynamically stable one, its energy being 4.52 kcal/mol lower than that of isomer **2b**. These results are in qualitative agreement with the difference in reactivity of the two isomeric dimers.

It is worth noting that if one considers the nonsilylated dimers, it appears that the cyclization should occur with the same facility in the two cases: the energy of the meso and threo dimers without silicon being respectively 13.24 and 13.43 kcal/mol with the same 3.44-Å cyclization distance. These values show that the difference of behavior between **2a** and **2b** comes from the steric hindrance brought by the silicon group which prevents **2a** from undergoing a spontaneous cyclization.

Silylation Orientation. Silylation presumably proceeds by electron transfer leading to anion radical intermediates as previously proposed for naphthalene[17] or quinoline.[4] It is worth noting that quinoline, when treated with the $Me_3SiCl/Li/THF$ reagent gave tetra- and hexa-

(13) Palmer, D. C.; Strauss, M. J. *Chem. Rev.* **1977**, *77*, 1.
(14) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127.
(15) Stewart, J. J. P. *J. Comput.-Aided Mol. Des.* **1990**, *4*, 1.
(16) Dewar, M. J. S.; Thiel, W. *J. Am. Chem. Soc.* **1977**, *99*, 4899.
(17) Weyenberg, D. R.; Toporcer, L. H. *J. Org. Chem.* **1965**, *30*, 943; *J. Am. Chem. Soc.* **1962**, *84*, 2843. Laguerre, M.; Dunogues, J.; Calas, R. *Tetrahedron Lett.* **1981**, *22*, 1227.

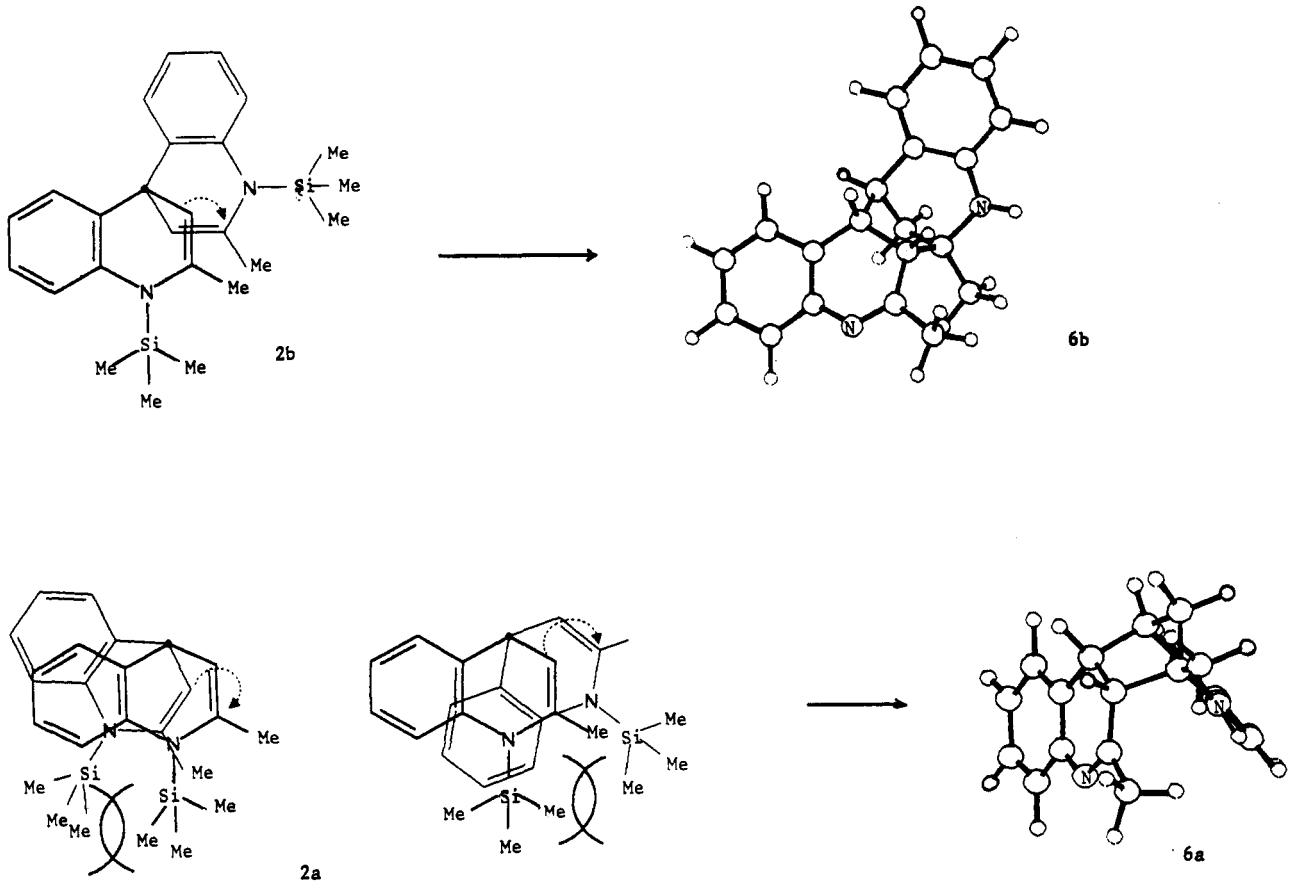
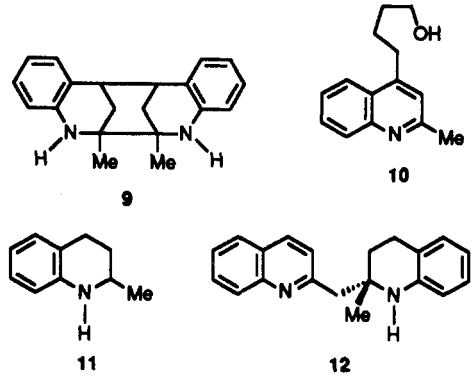


Figure 3. Schematic drawings of the cyclization conformation for **2b** and **2a** (two possibilities) showing the severe hindrance in **2a** (black dot is the C-4–C-4′ bond) and geometry of the cyclized products **6b** and **6a**.

Scheme V



silylated products but no dimer. In this case, highly silylated products were assumed to arise from the 1,2-disilyl derivatives. Results obtained on quinaldine confirm this hypothesis; introduction of the methyl group hinders binding of silicon in position 2 and prevents tetra- and hexasilylation. The fact that disilylation is more efficient with lithium than with magnesium is in agreement with their respective reductive power.[18] The regiochemistry of disilylation and the stereochemistry of dimerization depending on the metal involved are notable, but difficult to rationalize, in particular the fact that the thermodynamically less stable dimer is obtained when magnesium is used in boiling THF and the more stable one with lithium at 0 °C. Solvation phenomena, salt effects, or different structures for the reaction intermediate depending on the metal could play an important role. In particular, the mechanism of dimerization only involving a radical duplication can be ruled out considering the results obtained by T. N. Mitchell[19] with pyridine derivatives using disilylmercurial. In this case, the reaction has been shown to proceed radically leading to a 50/50 mixture of dimer isomers. It is worth noting that Becker et al. also obtained a *N*-silyl dimer when using the same reagent with quinoline,[3a] but no precision was given concerning the stereochemistry. With Me_3SiCl/metal/THF reagents, the attack of a quinaldine molecule by a *N*-silyl anion or a dianion could explain the experimental results, since the nature of the associated cation is responsible for the dimerization stereochemistry. At the moment, we cannot predict if the N-silylation step took place prior to the duplication leading to an *N*-silyl anion or after. The mechanism involving an *N*-silyl anion is depicted in Scheme VI. Studies of other substrates are now in progress to attempt to interpret the mechanism of silylation.

Experimental Section

Melting points were determined on a Metler capillary apparatus and are uncorrected.

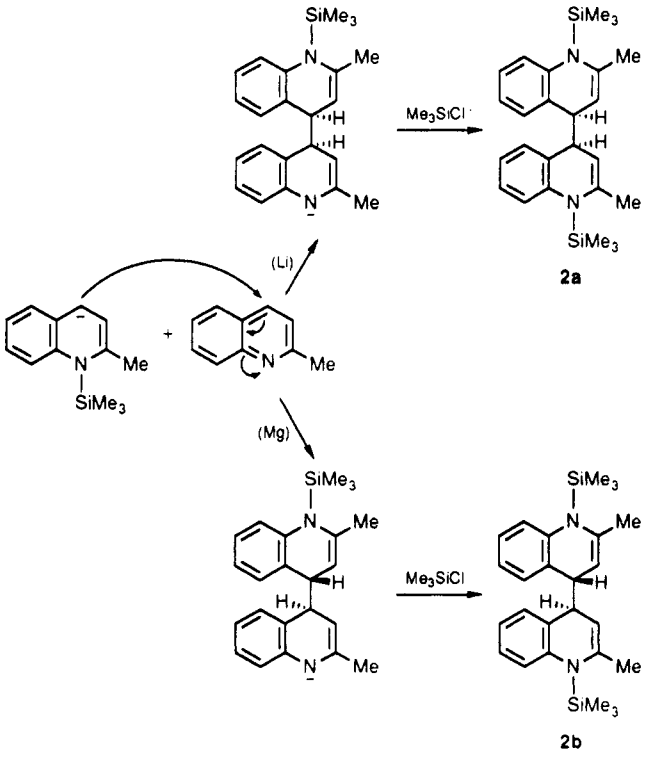
IR spectra were obtained on a Perkin-Elmer 457 spectrophotometer. The NMR spectra were recorded on Perkin-Elmer Hitachi R 24A (60 MHz) and Bruker AM 250 and WH 500 instruments. Mass spectra were measured on an AEI MS 12 spectrometer. Elemental analyses were performed by ATX Society in Nanterre, France.

Materials. Unless specified otherwise, reagent grade chemicals were used as received. Lithium wire obtained commercially

(18) Calas, R.; Duffaut, N.; Biran, C.; Bourgeois, P.; Pisciotti, F.; Dunogues, J. *C. R. Acad. Sci. Fr.* **1968**, *267 C*, 1968. Dunogues, J.; Calas, R.; Boulourtchian, M.; Biran, C.; Duffaut, N. *J. Organomet. Chem.* **1973**, *57*, 55. Dunogues, J.; Ekouya, A.; Calas, R.; Duffaut, N. *J. Organomet. Chem.* **1975**, *87*, 151.

(19) Mitchell, T. N. *J. Chem. Soc., Perkin Trans. II* **1976**, 1149.

Scheme VI



(Aldrich 1% Na) was granulated in Vaseline oil prior to use. Tetrahydrofuran was distilled from sodium benzophenone ketyl and degassed before use by an ultrasonic cleaning bath. All the reactions were carried out under argon by employing vacuum line techniques.

Silylation by $Me_3SiCl/Li/THF$: Typical Procedure. To a vigorously stirred cooled suspension of granulated lithium (0.4 g, 5.6 10^{-2} g·atom) in THF (100 mL) and freshly distilled trimethylchlorosilane (7.9 g; 73 mmol) was added to a solution of quinaldine (4 g, 28 mmol) in THF (20 mL) within 0.5 h. During addition, the temperature was kept below 5 °C. The solution was then stirred 2.5 h at this temperature. THF was partially evaporated and cyclohexane (50 mL) was added. The resulting precipitate of lithium chloride was removed by filtration and the solvents were evaporated. This operation had to be repeated once to allow complete elimination of lithium chloride. Treatment of the resulting oil with cyclohexane (40 mL) gave after 5 h a white solid (**2a**, 2.8 g; 23%). Crystallization from hexane gave the pure dimer **2a**. Distillation of the cyclohexane solution under reduced pressure provided 1 as a pale yellow oil (5.3 g; 66%).

A number of experiments in which this typical process was modified were carried out; they always led to the same products with only a little variation in yields: when the reaction mixture was not cooled during the addition of quinaldine (temperature rose to 20 °C), 1 and **2a** were isolated in yields of 68% and 20% respectively; dropwise addition of Me_3SiCl instead quinaldine led to 1 (55%) and **2a** (30%); and using 1 equiv of lithium (0.2 g, 2.8 10^{-2} g·atom) instead of two and Me_3SiCl (3.9 g, 36 mmol) gave 1 (2.3 g; 29%) and **2a** (2.4 g; 20%) besides unreacted starting material (1.6 g; 40%).

1,4-Bis(trimethylsilyl)-1,4-dihydroquinaldine (1): bp 106–108 °C (0.1 Torr); IR (neat, cm^{-1}) 3040, 3020, 1650, 1590, 1570, 1480, 1445, 1370, 1315, 1305, 1250, 1180, 1165, 1110, 1060, 1040, 1000, 840, 740, 680, 620; ^1H NMR (250 MHz, $CDCl_3$) δ 7.0 (d, 1 H, J = 7.3 Hz), 6.7–6.9 (m, 3 H), 4.85 (d, 1 H, J = 6.8 Hz), 2.7 (d, 1 H, J = 6.8 Hz), 2.0 (s, 3 H), 0.4 (s, 9 H), 0.05 (s, 9 H); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 136.7, 133.8, 127.1, 124.2, 121.4, 120.0, 106.1, 27.0, 25.4, 2.9, –2.4. Anal. Calcd for $C_{16}H_{27}NSi_2$: C, 66.36; H, 9.40; N, 4.84. Found: C, 66.28; H, 9.37; N, 4.69.

***N,N'*-Bis(trimethylsilyl)-1,1',4,4'-tetrahydro-4,4'-biquinaldine (2a)**: mp 199 °C (hexane); IR (neat, cm^{-1}) 1580, 1250, 850; ^1H NMR (250 MHz, CD_2Cl_2) δ 7.1 (m, 2 H), 6.9 (m, 3 H), 4.65 (m, 1 H), 3.05 (dd, 1 H, J = 2.1, 4.4 Hz), 2.05 (d, 3 H, J = 1.1 Hz), 0.4 (s, 9 H); ^{13}C NMR (62.86 MHz, CD_2Cl_2) δ 145.8, 141.05, 131.8, 129.6, 125.1, 121.2, 120.8, 109.4, 43.3, 22.2, 2.6; MS (EI) m/z (rel intensity) 216 (M/2, 20), 144 (23), 143 (100), 128 (16), 115 (14), 75 (22), 73 (48). Anal. Calcd for $C_{26}H_{36}N_2Si_2$: C, 72.16; H, 8.39; N, 6.47. Found: C, 72.26; H, 8.42; N, 6.39.

4-(Trimethylsilyl)quinaldine (3) by Aromatization of 1. Air was passed for 24 h through a vigorously stirred solution of 1 (1 g, 3.5 mmol) in cyclohexane (10 mL) at room temperature. Aromatization was followed by thin layer chromatography (SiO_2; elution with CH_2Cl_2/C_6H_{12} 1:1). Solvant removal provided an oil, which was chromatographed on silica gel (elution with CH_2Cl_2/C_6H_{12} 4:6), affording 580 mg of **3** (77%): IR (neat, cm^{-1}) 3040, 3015, 1645, 1610, 1560, 1480, 1385, 1360, 1320, 1250, 1200, 1125, 840, 780, 750, 690, 640; ^1H NMR (250 MHz, $CDCl_3$) δ 7.94 (d, 1 H, J = 8.3 Hz), 7.85 (d, 1 H, J = 8.3 Hz), 7.5 (dd, 1 H, J = 8.3, 7.2 Hz), 7.3 (dd, 1 H, J = 8.3, 7.2 Hz), 7.2 (s, 1 H), 2.6 (s, 3 H), 0.3 (s, 9 H); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 157.3, 148.4, 147.0, 129.7, 128.8, 128.5, 127.4, 125.1, 25.05, –0.5. Anal. Calcd for $C_{13}H_{17}NSi$: C, 72.50; H, 7.96; N, 6.50; Si, 13.04. Found: C, 72.45; H, 7.95; N, 6.53; Si, 12.85.

Silylation by $Me_3SiCl/Mg/THF$. Trimethylchlorosilane (7.9 g; 73 mmol) was added slowly (0.5 h) to a suspension of magnesium powder (1 g) in THF (120 mL) and quinaldine (4 g, 28 mmol) heated at reflux. The reaction mixture was then heated for an additional 2.5 h. Most of the THF was removed in vacuo and cyclohexane (50 mL) was added. The mixture was filtered to remove magnesium chloride and the solvents were evaporated. Cyclohexane (50 mL) was added again and the filtration repeated. Removal of the solvent provided 11 g of an oil. This oil constituted of two compounds was not allowed to stand for prolonged periods and was treated with methanol without purification (see below).

3-(Trimethylsilyl)quinaldine (5). When the silylation mixture obtained with magnesium was distilled in vacuo to allow isolation of the disilylated product, 1.6 g of **5** (20%) was obtained. Attempt to acylate this silylation mixture (5 g) with acetyl chloride (4.4 g, 56 mmol) in 50 mL of benzene at 0 °C also gave compound **5** in 18% yield beside 7 (40%), identical in all respects to the sample obtained by reaction with methanol (see experimental details below). **5**: IR (neat, cm^{-1}) 3040, 3020, 1650, 1610, 1560, 1540, 1480, 1390, 1360, 1320, 1250, 1220, 1200, 1130, 840, 780, 750, 690, 640; ^1H NMR (250 MHz, $CDCl_3$) δ 8.1 (s, 1 H), 7.9 (d, 1 H, J = 8.3 Hz), 7.63 (dd, 1 H, J = 1, 8.1 Hz), 7.56 (dt, 1 H, J = 1.4, 7.7 Hz), 7.35 (t, 1 H, J = 7.5 Hz), 2.74 (s, 3 H), 0.3 (s, 9 H); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ ppm 162.4, 147.7, 143.6, 132.3, 129.8, 128.2, 127.5, 126.1, 125.7, 27.0, –0.4. Anal. Calcd for $C_{13}H_{17}NSi$: C, 72.50; H, 7.96; N, 6.50. Found: C, 72.39; H, 7.99; N, 6.38.

6a,7,13,13a-Tetrahydro-6,7-dimethyl-7,13-methano-8*H*-quino[3,4-*c*][1]benzazepine (6b). The oil obtained with magnesium as described above (11 g) was dissolved in methanol (50 mL) and stirred at room temperature for 15 min, leading to the precipitation of a white solid. Filtration gave **6b** (9.2 g; 76% yield based on quinoline): mp 135 °C (EtOH); IR (neat, cm^{-1}) 3400, 3250, 3050, 3010, 2950, 2850, 1625, 1600, 1580, 1480, 775, 750, 740; ^1H NMR (250 MHz, CD_2Cl_2) δ 7.1 (m, 5 H), 6.3 (m, 3 H), 3.8 (NH), 3.7 (dd, 1 H, J = 5.9, 13.4 Hz), 3.3 (m, 1 H), 2.9 (d, 1 H, J = 13.4 Hz), 2.2 (s, 3 H), 2.0 (m, 1 H), 1.9 (m, 1 H), 1.7 (s, 3 H); ^{13}C NMR (62.86 MHz, CD_2Cl_2) δ 143.0, 141.0, 136.0, 129.3, 127.7, 127.2, 126.8, 126.5, 125.5, 125.1, 124.8, 116.7, 113.5, 53.3, 48.5, 47.2, 39.5, 27.9, 27.1; MS (EI) m/z (rel intensity) 288 (M^+, 13), 287 (18), 286 (6), 146 (32), 145 (21), 144 (100), 143 (23), 130 (32). Anal. Calcd for $C_{20}H_{20}N_2$: C, 83.30; H, 6.99; N, 9.71. Found: C, 83.31; H, 6.91; N, 9.52.

Evaporation of the methanol solution gave 1.3 g of intractable tars showing no $SiMe_3$ signal in ^1H NMR.

7,13,-Dihydro-6,7-dimethyl-7,13-methano-8*H*-quino[3,4-*c*][1]benzazepine (7). A suspension of **6b** (4.9 g, 17 mmol) in methanol (20 mL) was stirred at room temperature. The solid slowly disappeared and was completely dissolved after 24 h. Removal of methanol gave 7 (4.8 g; 99%). It was crystallized from ligroin (bp 90–120 °C): mp 207 °C; IR (neat, cm^{-1}) 3400, 3250, 3040, 3000, 2940, 2900, 1590, 1560, 1540, 1490, 1460, 1405, 760, 740, 660, 640; ^1H NMR (500 MHz, CD_2Cl_2) δ 8.1 (dt, 1 H, J = 8.2, 0.9 Hz), 8.0 (d, 1 H, J = 8.5 Hz), 7.6 (dt, 1 H, J = 7.0, 1.5 Hz), 7.56 (t, 1 H, J = 7.95 Hz), 7.2 (dd, 1 H, J = 7.5, 1.4 Hz), 7.0 (t, 1 H, J = 7.7 Hz), 6.7 (t, 1 H, J = 7.4 Hz), 6.5 (d, 1 H, J = 8 Hz), 4.5 (d, 1 H, J = 4.3 Hz), 4.2 (NH), 2.8 (s, 3 H), 2.4 (dd, 1 H, J = 10.5, 4.3 Hz), 2.1 (d, 1 H, J = 10.5 Hz), 1.9 (s, 3 H); ^{13}C

NMR (125.72 MHz, CD_2Cl_2) δ 153.4, 149.4, 147.5, 141.6, 130.5, 128.7, 128.6, 127.9, 126.3, 125.9, 124.1, 123.4, 122.1, 117.8, 115.5, 61.8, 44.0, 41.6, 24.6, 24.3; MS *m/z* (rel intensity) 286 (M^+, 2), 144 (27), 143 (100), 128 (16), 115 (13). Anal. Calcd for $C_{20}N_{18}N_2$: C, 83.90; H, 6.29; H, 9.79. Found: C, 83.78; H, 6.32; N, 9.71.

Methanolysis of Dimer 2a. The meso dimer **2a** (2 g; 4.6 mmol) was dissolved in a mixture of methanol (40 mL) and HMPT (8 g, 4.5 mmol). This solution was stirred for 40 h at room temperature. After removal of the methanol, the oily residue was dissolved in ether, washed with water, and then dried on sodium sulfate. Solvent was removed in vacuo and the crude product was chromatographed on silica gel. Elution with dichloromethane gave 2.3 g of 4,4′-biquinaldine (**8**) (18%): mp 242 °C (hexane–acetone), lit.[10] mp 242–244 °C; ^1H NMR (60 MHz, $CDCl_3$) δ 8.15–7.2 (m, 10 H), 2.85 (s, 6 H). Anal. Calcd for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85. Found: C, 84.42; H, 5.59; N, 9.71.

Elution with 20% ether in dichloromethane gave 850 mg of **7** (65%) identical with the sample obtained from **2b**.

Reaction of Quinaldine with Lithium in Tetrahydrofuran. To a vigorously stirred cooled suspension of granulated lithium (0.4 g; 5.6 10^{-2} g·atom) in THF (30 mL) was added a solution of quinaldine (4 g, 28 mmol) in THF (20 mL). During addition, the temperature was kept below 5 °C. The solution was then stirred 96 h at this temperature. The lithium excess was removed by filtration and the reaction mixture was poured into cold water. The hydrolysate was extracted with methylene chloride and washed with water. After removal of the solvent, cyclohexane (50 mL) was added to the residue. After a night an insoluble oil was separated (1.3 g). It was chromatographed on silica gel, giving **10** (210 mg, 5%), **11** (170 mg, 4%), and quinaldine (300 mg, 8%) in addition to **7** (500 mg, 13%) identical to the sample obtained from **2b**. The cyclohexane layer gave after evaporation of the solvent, an unstable product (900 mg) which evolved, leading to **7** (830 mg, 21%). The reaction products impregnated on lithium excess were extracted with methylene chloride after hydrolysis. The organic layer was washed with water and then dried on magnesium sulfate. After evaporation of the solvent, a solid appeared by addition of chloroform. It was filtered off and identified as **6b** (110 mg, 3%). The remaining solution was evaporated and the crude product (1.2 g) was chromatographed on silica gel, leading to quinaldine (960 mg, 24% yield) and **7** (280 mg, 7%).

When the reaction was stopped after 12 h of stirring at 0 °C, we obtained quinaldine (2 g, 50%), **7** (700 mg, 18%), **12** (300 mg, 8%) and 700 mg of intractable tars.

Quinaldine-4-butanol (10): IR (neat, cm^{-1}): 3300, 3050, 2950, 2850, 1590, 1560, 1500, 1405, 1370, 1060; ^1H NMR (250 MHz, $CDCl_3$) δ 7.77 (d, 1 H, *J* = 8.4 Hz), 7.66 (d, 1 H, *J* = 8.3 Hz), 7.35 (t, 1 H, *J* = 7.3, 7.8 Hz), 7.17 (t, 1 H, *J* = 7.7, 7.4 Hz), 6.78 (s, 1 H), 3.46 (t, 2 H, *J* = 6.3, 6.0 Hz), 2.71 (t, 2 H, *J* = 6.9, 7.7 Hz), 1.54 (m, 2 H), 1.45 (m, 2 H), 2.37 (s, 3 H); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 158.1, 148.6, 147.1, 128.9, 128.3, 125.5, 125.3, 123.1, 121.3, 61.4, 32.3, 31.5, 26.0, 24.6; MS (EI) *m/z* (rel intensity) 215 (M^+, 100), 182 (26.3), 171 (18.6), 170 (52.3), 169 (36.7), 168 (27), 167 (8.6), 158 (16), 157 (69.9), 156 (42.7), 144 (79), 143 (17.5), 129 (12.5), 128 (16.5), 116 (11.4), 115 (30.6), 77 (10.2), 31 (11.1).

1,2,3,4-Tetrahydroquinaldine (11): IR (neat, cm^{-1}) 3400, 3050, 2950, 2850, 1600, 1580, 1490, 1310; ^1H NMR (250 MHz, $CDCl_3$) δ 7 (m, 2 H), 6.64 (dt, 1 H, *J* = 7.3, 1.2 Hz), 6.5 (dd, 1 H, *J* = 8.5, 1.1 Hz), 3.45 (NH), 3.42 (m, 1 H), 2.81 (m, 2 H), 1.97 (m, 1 H), 1.63 (m, 1 H), 1.24 (d, 3 H, *J* = 6.3 Hz); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 144.7, 129.2, 126.6, 121.1, 116.9, 113.9, 42.1, 30.1, 26.5, 22.6; MS (EI) *m/z* (rel intensity) 147 (M^+, 36.8), 146 (6.4), 143 (4.5), 133 (10.1), 132 (100), 131 (5.1), 130 (10.1), 117 (11), 77 (8), 66 (7.7), 65 (7.1).

1,2,3,4-Tetrahydro-2-(2-quinolylmethyl)quinaldine (12): IR (neat, cm^{-1}) 3400, 3050, 2990, 2920, 2900, 1590, 1550, 1480, 1420, 1305, 1260; ^1H NMR (250 MHz, $CDCl_3$) δ 8.2 (d, 1 H, *J* = 8.4 Hz), 8.09 (q, 1 H, *J* = 6.5 Hz), 7.8 (d, 1 H, *J* = 7.6 Hz), 7.7 (m, 1 H), 7.56 (t, 1 H, *J* = 7.8, 7.2 Hz), 7.23 (d, 1 H, *J* = 8.4 Hz), 7.11 (m, 2 H), 6.73 (dt, 1 H, *J* = 7.3, 7.4, 1.1 Hz), 7.68 (dd, 1 H, *J* = 8.1, 1.1 Hz), 4.7 (NH), 3.18 (syst AB, 2 H, *J* = 13.1 Hz), 2.90 (q, 2 H, *J* = 6.5 Hz), 1.86 (dt, 2 H, *J* = 6.8, 1.7 Hz), 1.18 (s, 3 H); ^{13}C NMR (62.86 MHz, $CDCl_3$) δ 159.4, 147.9, 144.0, 135.7, 129.3, 129.2, 127.4, 126.7, 126.5, 125.7, 123.1, 120.3, 116.5, 114.6, 51.8, 48.5, 33.9, 23.4, 25.2; MS (EI) *m/z* (rel intensity) 288 (M^+, 1.3), 146 (15), 143 (100), 132 (21), 128 (13), 115 (11).

Quantum Mechanics. All calculations were performed on a local DEC network consisting of a Micro-Vax II and a Micro-Vax 3100 running the July 1991 version of CHEM-X (Chemical Design Ltd., Oxford). The X-ray coordinate file of **2a** was transferred into CHEM-X and converted into CSSR format. The C-4–C-4′ bond was then rotated by 30° steps and the "cyclization" distance (C-2···C-3′ or C-3···C-2′) checked. The conformers giving the shortest distances were selected and their files written into the CSSR format. For the stereoisomer **2b**, the chirality of one of the asymmetrical carbon atoms in **2a** was inverted and the same procedure as above was then applied. All these files were introduced in the MOPAC version 6.0 module[15] implemented in the CHEM-X software. A CPU time limit of 5000 min (T = 5000M as keyword) was specified. In the particular case of **2a** conformers, it was necessary to override the geometry checks by invoking the keyword GEO-OK. All calculations were done while enabling a full geometry optimization using the full Z-matrix.

X-ray Crystallography of Compounds 2a and 7. Transparent colorless crystals were obtained at room temperature from hexane (**2a**) or ligroin (**7**) solution. A single crystal was selected for intensity data collection on an Enraf-Nonius CAD-4 diffractometer. The data were measured with the ω–2θ scan technique with a variable scanning rate, using graphite-monochromated Cu Kα radiation. Two standard reflections measured every 5400 s of radiation time showed no significant variation. The intensities were corrected for Lorentz and polarization effects but not for absorption.

The structures were solved by direct methods using the MULTAN 80 program[20] and electron density synthesis. Difference Fourier maps revealed the hydrogen atoms. Block-diagonal matrix least-squares refinements were performed for a scale factor, positional, and anisotropic thermal parameters of the non-hydrogen atoms. The hydrogen atoms were included in the calculations and refined with isotropic thermal parameters. The function minimized was $w||F_o| - |F_c||$ where $w = 1$ if $|F_o| < P$, $P = [F_o(\max)/10]$, $w = (P/F_o)$ if $|F_o| > P$. The scattering factors used for non-hydrogen atoms were taken from the ref 21 and for hydrogen atoms from Stewart et al.[22] All calculations were performed on a Mini 6-92 CII-Honeywell Bull computer using unpublished programs from the Laboratoire de Cristallographie, University of Bordeaux I (33400 Talence, France).

Experimental details are given in Table II (supplementary material). Atomic parameters of each crystal are given in Table III (supplementary material). The molecules and their atom numbering scheme are shown in Figures 1 and 2 (supplementary material).

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Supplementary Material Available: X-ray data for compounds **2a** and **7** (10 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(20) Main, P.; Hull, S. E.; Lessigner, L.; Germain, G.; Declercq, J.-P.; Woolfson, M. M. MULTAN 80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data, Universities of York, England, and Louvain, Belgium, 1978.

(21) *International Tables for X-ray Crystallography*, Vol. IV; Kynoch Press: Birmingham (Present distributor: D. Reidel, Dordrecht), 1974.

(22) Stewart, R. F.; Davidson, E. R.; Simpson, W. T. *J. Chem. Phys.* **1965**, *42*, 3175.