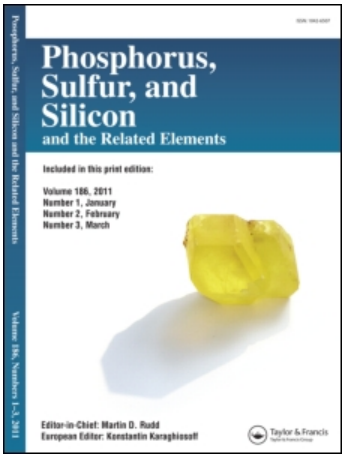

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SYNTHESIS OF NOVEL C-ORGANOSILICON DERIVATIVES, POTENTIAL INHIBITORS OF HIV REVERSE TRANSCRIPTION

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SYNTHESIS OF NOVEL C-ORGANOSILICON DERIVATIVES, POTENTIAL INHIBITORS OF HIV REVERSE TRANSCRIPTION

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(Received December 8, 1994; in final form January 19, 1995)

A series of silylated nucleobases was synthesized as potential therapeutic agents against HIV. These compounds were designed to interact with the active site of HIV Reverse Transcriptase (RT). Such molecules might therefore inhibit the reverse transcription process of the virus.

Key words: Nucleobases, silanols, siloxane 2D-NMR, HIV, reverse transcriptase.

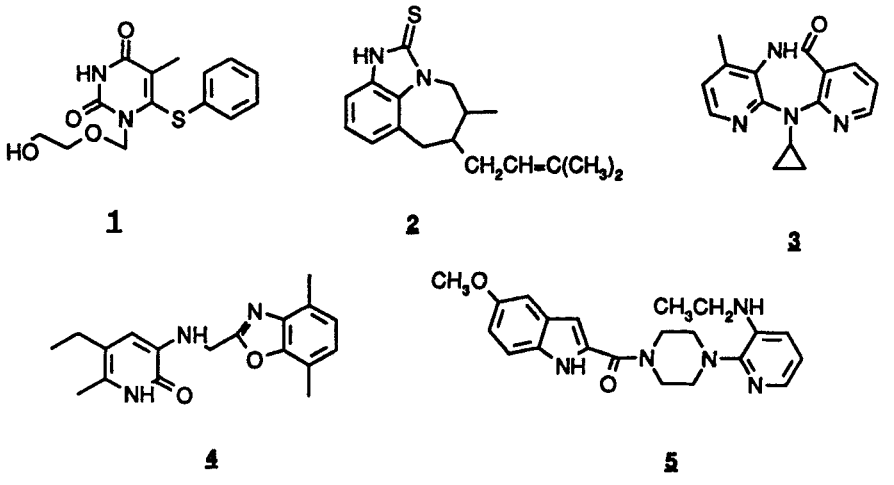
INTRODUCTION

There is considerable interest in the use of human immunodeficiency virus (HIV) reverse transcriptase as a target for the treatment of AIDS.[1] Azido thymidine (AZT)[2] and dideoxyinosine (DDI),[3] so far the only drugs approved for the clinical treatment of AIDS are potent terminators of DNA chain elongation during the HIV-1 reverse transcription process. Rapid mutations in the viral genome however, lead to the emergence of drug-resistant strains. Furthermore, they also induce severe side effects, including bone marrow suppression (AZT), peripheral neuropathy or pancreatitis (DDI) and others, necessitating the search for more satisfactory compounds. Although some new compounds have been described since then—acyclouridine **1** (HEPT),[4] benzodiazepinone **2** (TIBO),[5] dipyridodiazepinone[6] **3**, pyridinone[7] **4** and bis(heteroaryl)piperazine **5** (BHAP)[8]—they act as specific inhibitors of the HIV reverse transcriptase rather than DNA chain terminators (Scheme 1).

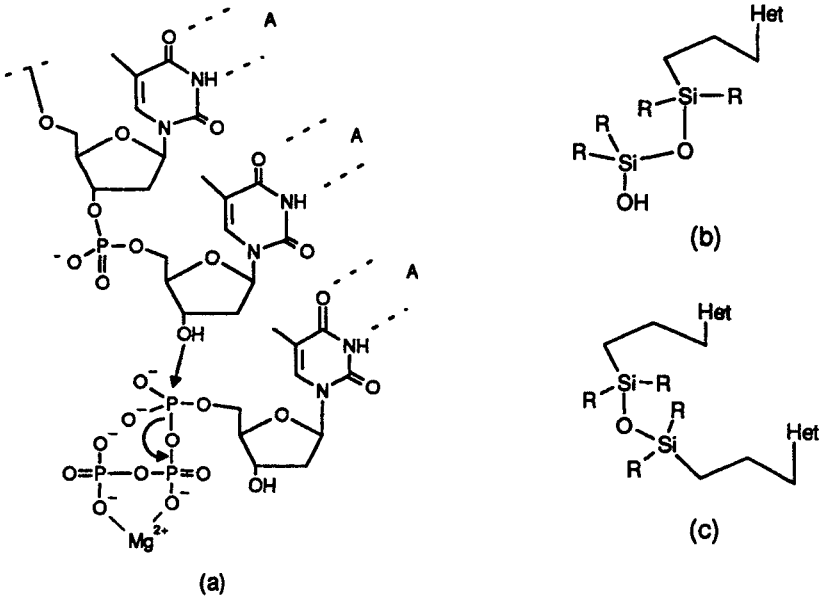
Actually, the transition state of the catalysed reaction is supposed to proceed through a nucleophilic attack of the 3′-terminal hydroxyl group of DNA, on the α-phosphorus of the newly added nucleoside triphosphate (Scheme 2a). In this pattern, the phosphorus atom undergoes a valence extension from the tetravalent to the pentavalent state, before the expulsion of the diphosphate moiety.[9]

We would like here to describe the synthesis of organosilicon derivatives which could interact with the catalytic site of the RT using two strategies of medicinal chemistry:

—Synthesis of transition state analogues[10] (Scheme 2b); such compounds require a heterocycle able to generate hydrogen bonds with the complementary RNA strand, an atom which readily accepts the nucleophilic attack (as does phos-



SCHEME 1



SCHEME 2 (a) Incorporation of a nucleotide in the growing DNA strand catalysed by the retroviral DNA polymerase (Reverse Transcriptase): A = adenine; (b, c) General structure of the organosilicon compounds synthesized (R = Me, Phe; Het = heterocycle).

phorus) and retains relative stability when pentavalent. Due to the low energy state of its 3d orbitals and its similarity with phosphorus in term of bond length and bond angles, the silicon atom is a good candidate.

—Synthesis of bisubstrate analogues[11] (Scheme 2c).

Thus, a series of silanols, siloxanes, or silanol-siloxanes bearing one or two heterocycles with a variable length of the hydrocarbon chain between the heterocycle and the silicon atom was synthesized.

RESULTS

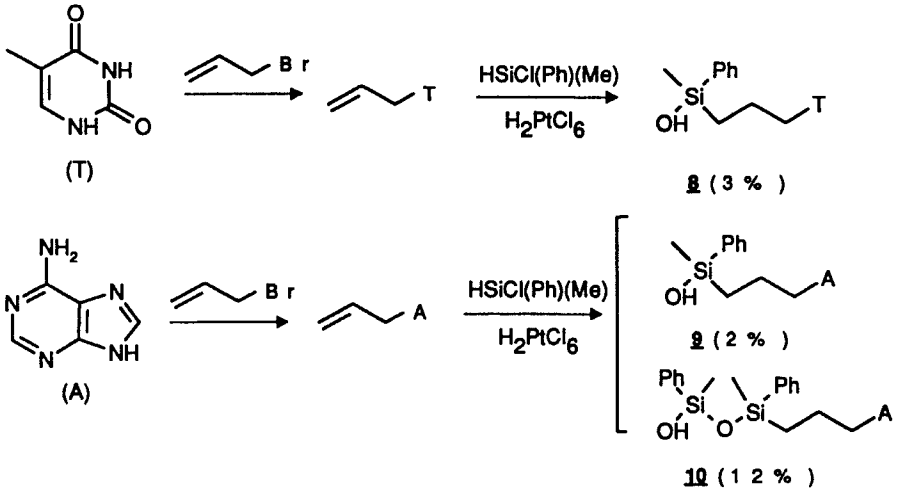
Molecules bearing one thymine or adenine nucleobases were obtained by a hydrosilylation reaction. Condensation of allylbromide on thymine and adenine sodium salts[12] yielded N-1-allylthymine and N-7-allyladenine which upon hydrosilylation with phenylmethylchlorosilane in the presence of Speier's catalyst[13] gave the silylated compounds **8**, **9** and **10** (Scheme 3). The low yields observed can be explained by the poor solubility of the nucleobases in non polar solvents required for the organochlorosilanes; furthermore, we could not prevent the reduction of N-allyladenine and N-allylthymine to N-propyladenine and N-propylthymine during the reaction.

Molecules embodying two heterocycles were obtained by condensation of various heterocyclic sodium salts on either 3-(chloropropyl)dimethylchlorosilane **11**, 4-(chlorobutyl)dimethylchlorosilane **12**, or 1,3-bis(3-chloropropyl)-1,1,3,3-tetramethyldisiloxane **13** according to Scheme 4.

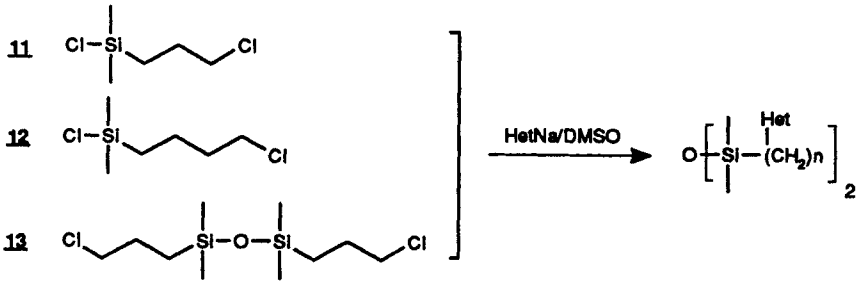
Results are reported in Table I.

With thymine, in any case, a competition between N-1 and N-3 alkylation was observed, as previously mentioned in the literature.[14] Reactions yielded only a small ratio (ca 5%) of N-3, N-3′ bis-alkylation adducts, which were readily separated by washing with ether. However, even with a good crude yield, (100% and 67% with an equimolar ratio of **15/17** and **16/18** respectively), attempts to obtain pure compounds were difficult, and the ratio of **15/17** and **16/18** was raised to 8/2, but with a dramatic fall in the yield (18 and 5% respectively). An alternative with 3-(chloropropyl)tetramethyldisiloxane according to Vorbruggen's method[15] was ineffective.

Reaction on adenine yielded **19** and **20**. Furthermore, both N-7 and N-9 regioisomers **21** and **22** were formed (with respective yields of 40% and 67%, ratio 8/2). As previously described in the literature,[16] N-9/N-7 ratio for alkylation is close to



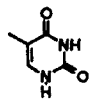
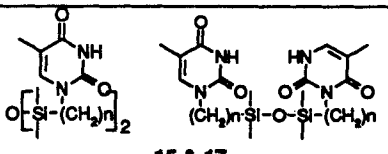
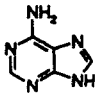
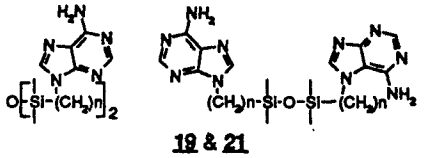
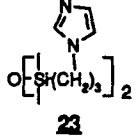
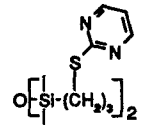
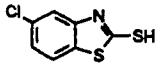
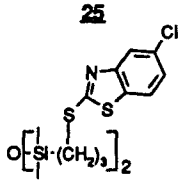
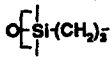
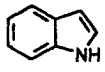
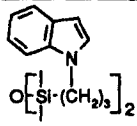
SCHEME 3 (T: thymine, A: adenine).



SCHEME 4

TABLE I

Condensation of heterocyclic sodium salts with **11**, **12**, and **13**

Organosilicon derivative	Heterocycle	Products	Yield
Cl-Si(CH$_2$)n-Cl **11** : n=3 **12** : n=4		 **15** & **17** **16** & **18**	n= 3: **15** & **17** (8/2, 18%) n= 4: **16** & **18** (8/2, 5%)
		 **19** & **21** **20** & **22**	n= 3: **19** & **21** (8/2, 40%) n= 4: **20** & **22** (8/2, 60%)
Cl-Si(CH$_2$)n-Cl **11** : n=3		 **23**	(59%)
		 **25**	(47%)
		 **26**	(21%)
 **13**		 **24**	(27%)

9/1. Nevertheless, if **20** was isolated in a pure form after crystallisation (yield 26%), we were unable to obtain **19** free of its regioisomer **21**. On the other hand, heterocycles like imidazole, 2-mercaptopyridine, 5-chloromercaptobenzothiazole or 1H-indole were similarly used and lead to single compounds.

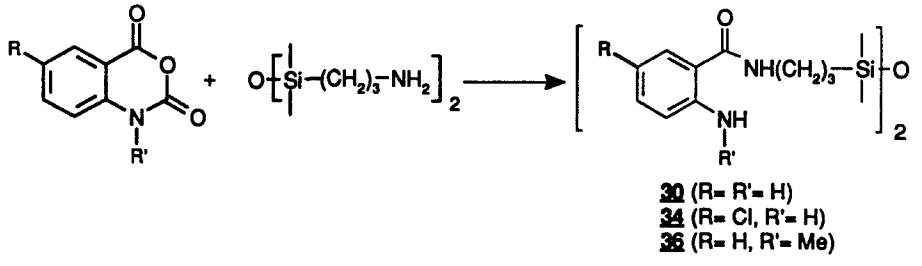
Finally, 1,3-bis(3-aminopropyl)-1,1,3,3-tetramethyldisiloxane **14** was caused to react with various isatoic anhydrides[17] (Scheme 5).

Results are reported in Table II.

Besides, the silylated aminobenzamides **30**, **34** were further cyclized to quinazoline derivatives according to Scheme 6.

Regioisomerism of the N-Alkylation for Thymine and Adenine Compounds

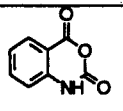
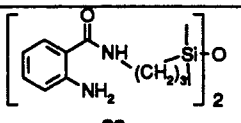
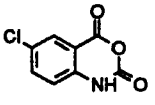
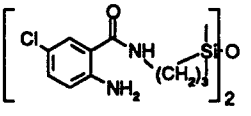
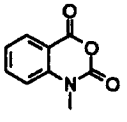
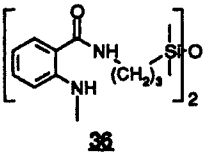
Alkylation of thymine on its N-1 position and adenine on its N-9 position was confirmed by means of 2D heteronuclear NMR techniques as similarly described for several substituted purine compounds.[18]

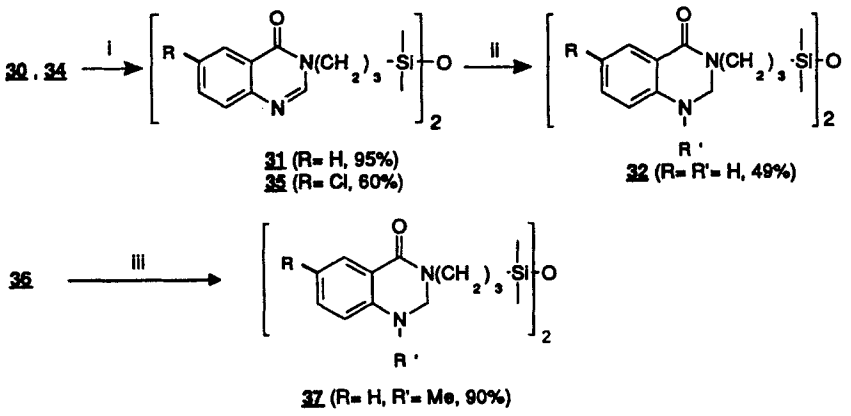


SCHEME 5

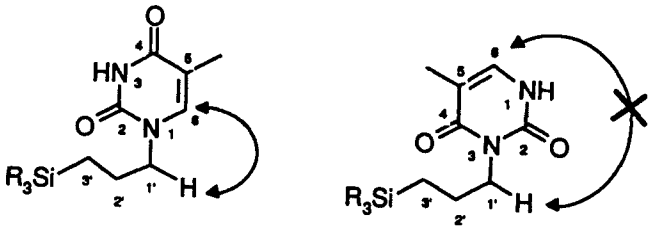
TABLE II

Condensation of **14** with isatoic anhydrides

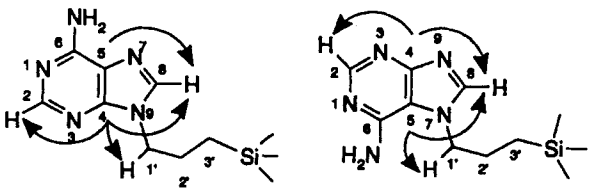
Organosilicon derivative	Heterocycle	Products	Yield
O[Si(CH2)3NH2]2 **14**		 **30**	(96%)
		 **34**	(74%)
		 **36**	(64%)



SCHEME 6 i) HCOOH, reflux; ii) $LiAlH_4$, Et_2O, reflux 3 days; iii) H_2CO, PhMe, reflux 5 h.



SCHEME 7 N-1 vs N-3 alkylation of thymine: ^3J H/C correlations.



SCHEME 8 N-9 vs N-7 alkylation of adenine: ^3J H/C correlations.

With thymine (compounds **15**) as the heterocycle, an HMQC (Heteronuclear Multiple Quantum Coherency)[19] experiment, revealed an H-6/C-6 correlation (δC_6 140.59 ppm) as the chemical shift of H-6 is unambiguous. Then a COSY experiment enabled us to identify the proton signals of the propyl chain, namely H-1′, by correlation starting with protons α- to silicon.

Finally, an HMBC (Heteronuclear Multiple Bound Correlation)[20] experiment revealed a ^3J H-1′/C-6 correlation only in accordance with N-1 alkylation of the thymine as N-3 alkylation would imply five bonds between H-1′ and C-6, a distance too long to observe any correlation (Scheme 7).

With adenine as the heterocycle (compound **10**), aromatic protons H-2 and H-8 are easily differentiated, and H-1′, H-2′ and H-3′ were identified using a COSY experiment as above.

HMBC technique revealed the following ^3J proton-carbon correlations pattern: H-2 H-1′ and H-8 with one carbon atom and H-8 with one other carbon atom. This pattern corresponds unambiguously to N-9 substituted adenine (three correlations with C-4 and one with C-5), as the correlation pattern of the N-7 substituted adenine would have been different (two correlations with C-4 and two with C-5, Scheme 8).

Thus, the chemical shifts for C-4 and C-5 are respectively δ = 149.00 and 119.00 ppm.

CONCLUSION

During this work we synthesized a series of novel organosilicon compounds designed to mimic the high energy species of the catalytic process performed by the RT of HIV. These compounds were tested as inhibitors of HIV-1 reverse transcriptase as well as inhibitors of HIV replication within virus infected lymphocytes. Full biological data will be submitted for publication elsewhere. Four of the synthesized derivatives were good inhibitors of the RT RNA dependent DNA polymerase activity of HIV-1 ($IC_{50} \approx 50$ μM). The RNaseH activity was much less affected (25% inhibition at 400 μM) as was cellular DNA α-polymerase (IC_{50} = 165–250 μM). One compound was found to be able to inhibit HIV-1 replication in virus infected lymphocytes. The level of activity was essentially the same on AZT sensitive (ID_{50} = 12.9 ± 1 μM) or AZT resistant strains (ID_{50} = 14.8 ± 0.5 μM).

EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. ^{1}H, ^{13}C and ^{29}Si NMR spectra were recorded on Bruker AC 200 (^{1}H: 200.13 MHz, ^{13}C: 50.32 Mhz) or Bruker AMX 500 (^{1}H: 500.13 MHz, ^{13}C: 125.76 Mhz, ^{29}Si: 99.36 MHz) instruments. Chemical shifts are given in ppm from tetramethylsilane as an internal standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Multiplicities in ^{13}C-NMR spectra were derived from DEPT or JMOD experiments. When necessary, COSY, HMQC and HMBC experiments were used. The chain between silicon atom and heteroatom (N or S) of the symmetrical compounds was numbered as follows: **N(S)-1′-2′-3′-Si** while current nomenclature was used for heterocycles. Infrared spectra were recorded on a Bruker IFS-25 FT IR instrument as KBr pellets or as solutions in the cited solvent. Patterns are designed as follows: br b, broad band; w b, weak band; sh, shoulder. Mass spectra were recorded on a Finnigan Mat TSQ 70 triplequadrupole mass spectrometer in electron impact ionization mode (70 eV). Thin-layer chromatography was performed on Merck silica gel 60 F-254 (0.25 mm thickness) plates. Column chromatography was performed on Silica gel 60 (230–400 mesh). All elemental analyses were performed by the Laboratoires du CNRS, Vernaison BP22, 69390, France.

8 *[3-(N-1-Thyminyl)propyl]methylphenylsilanol.* A solution of allylthymine (2g, 12 mmol) in anhydrous THF (10 ml) was added dropwise to a few drops of a 0.1 N chloroplatinic acid solution in isopropyl alcohol heated at 50°C, followed by addition of phenylmethylchlorosilane (1.88g, 12 mmol). The mixture was stirred at 50°C for 48h under inert atmosphere, allowed to cool to room temperature, then poured into a mixture of $NaHCO_3$ (1g, 12 mmol) and NH_4Cl (2g) and ice water (50 ml). The product was extracted with $CHCl_3$. The combined extracts dried over $MgSO_4$, filtered and concentrated under reduced pressure yielded an oil chromatographed on a silica gel column (CH_2Cl_2/MeOH: 95/5) to afford (**8**) as an oil (83mg, 3%) Rf: 0.40, dichloromethane/methanol: 90/10

IR (KBr), ν_{max} cm^{-1}: 3360 (br b, Si—O—H) and 3170 (br b, N—H), 3040 (C—H olefinic), 2950–2900 (C—H aliphatic), 1670 (br b, C=O and C=C), 1465, 1350; 1250, 850 and 760 (Me—Si); 1420 and 1110 (Ph—Si).

^{1}H-NMR ($CDCl_3$): 0.40 (s, 3H, Me—Si), 0.82 (m, 2H, H3'), 1.77 (m, 2H, H2'), 1.89 (s, 3H, Me—thy), 2.73 (br s, 1H, Si—OH), 3.68 (t, 2H, J = 7.3 Hz, H1'), 6.90 (s, 1H, H6), 7.47 (m, 3H ar), 7.55 (d, 2H ar), 8.45 (br s, 1H, H—N)

^{13}C-NMR ($CDCl_3$): −1.60 (Me—Si), 12.21 (Me—thy), 13.14 (C3'), 22.90 (C2'), 50.80 (C1'), 110.69 (C5), 127.86, 129.60, 133.17 (C—H ar), 137.87 (Si—C quat ar), 140.50 (C6), 151.25 (C2), 164.40 (C4).

9 *[3-(N-9-adenyl)propyl]methylphenylsilanol and* **10** *1-[3-(N-9-adenyl)propyl]methylphenyl-3-(methylphenyl)disiloxan-3-ol.* To a solution of allyladenine (1.93g, 11 mmol) in dry 1,2-dichloroethane was added under inert atmosphere phenylmethylchlorosilane (4.9 ml, 36 mmol) at 40°C followed, after 10 mn, by a few drops of chloroplatinic acid (0.10 N in isopropyl alcohol). The reaction was heated at 70–80°C for 7 days. After evaporation of the solvent, the remaining solution was washed with hot hexan to remove the excess of chlorosilane, then poured into a cold solution of ammonium chloride (50 ml). The product was extracted with $CHCl_3$, dried over $MgSO_4$ and filtered. The filtrate was evaporated and applied to a silica gel column (CH_2Cl_2/MeOH: 90/10) to yield a white powder (**9**, 70mg, 2%) and an oil (**10**, 590mg, 12%).

9: mp: 84°C; Rf: 0.20, dichloromethane/methanol: 90/10

IR (KBr), ν_{max} cm^{-1}: 3540 (sh Si—O—H), 3325 and 3175 (br b N—H), 2920 (C—H aliphatic), 1650, 1590, 1480; 1250, 860 and 736 (Me—Si); 1415 and 1110 (Ph—Si)

^{1}H-NMR ($CDCl_3$): 0.30 (s, 3H, Me—Si), 0.73 (m, 2H, H3'), 1.84 (m, 2H, H2'), 4.07 (m, 2H, H1'), 5.57 (br s, 2H, NH_2), 7.35 (m, 5H ar), 7.64 (d, H, H2 Ad), 8.33 (s, H, H8 Ad)

^{13}C-NMR ($CDCl_3$): −1.32 (Me—Si), 14.18 (C3'), 23.97 (C2'), 46.45 (C1'), 119.50 (C5), 127.87, 129.71, 133 (C—H ar), 137.41 (Si—C ar), 140.25 (C8), 150 (C4), 152.71 (C2), 155.63 (C6)

^{29}Si-NMR ($CDCl_3$): − 1.13

MS, m/z (%): 609 (M+, 7), 474.2 (5), 432 (100), 382 (15), 313 (2), 256.2 (3), 149 (17), 134.9 (7), this spectrum corresponds to the siloxane resulting from the silanol self condensation in the spectrometer source.

10: Two diastereoisomers Rf: 0.43, dichloromethane/methanol: 90/10

IR (KBr); ν_{max} cm^{-1}: 3540 (sh Si—O—H), 3325 and 3175 (br b N—H), 2920 (C—H aliphatic), 1650, 1590, 1480; 1250, 860 and 736 (Me—Si); 1428 and 1110 (Ph—Si), 1100–1000 (br b, Si—O—Si), 900 (Si—O—Si—OH)

^{1}H-NMR ($CDCl_3$): 0.33, 0.37, 0.40 and 0.42 (4s, 6H, CH_3—Si), 0.81 (m, 2H, H3'), 1.93 (m, 2H, H2'), 4.06 (m, 2H, H1'), 6.30 (s, 2H, NH_2), 7.32 (m, 6H, H ar), 7.60 (m, 4H, ar, H8), 8.22 (2s, 1H, H2)

^{13}C-NMR ($CDCl_3$): −0.94/−0.81 and −0.77/−0.74 (2 × 2 CH_3 − Si); 13.89 (C3'); 24.07 (C2'); 46.37/46.39 (2 C1'); 119.00 (C5); 127.69, 127.71, 127.77, 127.80, 129.50, 129.52, 1.29.70, 133.05, 133.26, 133.30 (C—H ar); 137.52, 137.63, 137.75, 137.84 (Si—C ar quat); 140.10 (C8); 149.00 (C4); 152.58 (C2); 155.60 (C6)

^{29}Si—NMR ($CDCl_3$): −1.66 and −1.73 (Si—C3'), −24.57 and −24.72 (Si—OH) MS, m/z (%): 449.1 (M+, 42), 434 (15), 194.8 (77), 149 (100), 136 (21).

13 *1,3-Bis[3-Chloropropyl]-1,1,3,3-tetramethyldisiloxane.*[6] A solution of (3-chloropropyl)dimethylchlorosilane **11**, (17.11g, 0.10 mol) in diethyl ether (10 ml), was slowly hydrolysed at 0°C with water. After stirring for 1 hr at room temperature, the organic layer was separated, dried over $MgSO_4$, then concentrated under reduced pressure to give the title compound (**13**, 14.37g, 100%); bp: 128°C/7 mm Hg; Rf: 0.78, dichloromethane

IR (KBr), ν_{max} cm^{-1}: 2950–2850; 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si)

^{1}H-NMR ($CDCl_3$): 0.10 (s, 6H, Me—Si), 0.63 (m, 2H, H3'), 1.80 (m, 2H, H2'), 3.53 (t, J: 7 Hz, 2H, H1'); ^{13}C-NMR ($CDCl_3$): 0.24 (Me—Si), 15.85 (C3'), 27.02 (C2'), 47.81 5 (C1').

Condensation on thymine. NaH (1.59g, 97% in oil, 64.25 mmol) was slowly added to a solution of thymine (8.47g, 67.15 mmol) in dry DMSO (80 ml) and the mixture was stirred for 2 h at 50°C. 3-(chloropropyl)dimethylchlorosilane (**11**, 4.8 ml, 29.21 mmol) was then added, and the mixture heated for 3 days at 100°C. The resulting solution was hydrolysed with water (300 ml) and extracted with CH_2Cl_2. The combined organic layers were washed with water and dried over $MgSO_4$. Evaporation gave a white powder washed with ether and recrystallised in MeOH to yield a mixture of **15** and **17** in an 80/20 ratio (1.20g, yield = 18%).

The same procedure was used starting from 4-(chlorobutyl)dimethylchlorosilane (**12**, 5.40 g, 29.21 mmoles) to give a mixture of **16** and **18** in an 80/20 ratio (0.33 g, yield = 5%).

15 (n = 3): Rf: 0.55, dichloromethane/methanol: 90/10.

IR and NMR spectra conducted on the mixture revealed the following signals in accordance with the expected structure.

IR (KBr), ν_{max} cm^{-1}: 3160 (N—H amide), 3050 (C—H olefinic), 2950–2800 (C—H aliphatic), 1680 (br b, C=O), 1350; 1250, 846 and 760 (CH_3—Si); 1100–1000 (br b, Si—O—Si)

^{1}H-NMR ($CDCl_3$): 0.03 (s, 6H, Me—Si), 0.46 (m, 2H, H3'), 1.65 (m, 2H, H2'), 1.90 (s, 3H, Me—thy), 3.65 (t, J: 7Hz, 2H, H1'), 6.95 (s, 1H, H6)

^{13}C-NMR ($CDCl_3$): 0.16 (Me—Si), 12.19 (Me—thy), 14.89 (C3'), 22.97 (C2'), 51.20 (C1'), 110.28 (C5), 140.59 (C6), 150.96 (C2), 164.59 (C4)

MS, m/z (%): 466.2 (M+, 2), 451.2 (4), 299.2 (87), 225.2 (99)

Anal. Calcd. for $C_{20}H_{34}N_4O_5Si_2$: C, 51.47; H, 7.29; N, 12.00. Found: C, 51.16; H, 7.33; N, 11.94.

16 (n = 4): Rf: 0.58 (dichloromethane/methanol: 90/10).

IR and NMR spectra conducted on the mixture revealed the following signals in accordance with the expected structure.

IR (KBr), ν_{max} cm^{-1}: 3160 (N—H amide), 3050 (C—H olefinic), 2950–2800 (C—H aliphatic), 1690 and 1650 (2 × br b, C=O), 1350; 1250, 840 and 760 (Me—Si); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.00 (s, 6H, Me—Si), 0.52 (m, 2H, H4'), 1.30 (m, 2H, H3'), 1.68 (m, 2H, H2'), 1.90 (s, 3H, Me—thy), 3.70 (t, J: 7 Hz, 2H, H1'), 6.96 (s, 1H, H6)

^{13}C-NMR ($CDCl_3$): 0.30 (Me—Si), 11.90 (Me—thy), 17.36 (C4'), 19.63 (C3'), 31.88 (C2'), 46.81 (C1'), 108.31 (C5), 141.41 (C6), 150.84 (C2), 164.22 (C4).

MS, m/z (%), 494 (M+, 2), 479.2 (4), 313.1 (66), 239.1 (26), 207 (12), 186 (13), 133 (19), 79 (100).

Anal. Calcd. for $C_{22}H_{38}N_4O_5Si_2$: C, 53.41; H, 7.74; N, 11.32. Found: C, 53.16; H, 7.33; N, 11.94.

Condensation on adenine. NaH (0.75g, 97% in oil, 26.4 mmol) was slowly added to a solution of adenine (3.72g, 27.6 mmol) in dry DMSO (15 ml) and the mixture was stirred to 2 h at 50°C. (3-chloropropyl)dimethylchlorosilane **11**, (2 ml, 12 mmol) was then added, and the mixture heated for 3 days at 50°C. The resulting solution was hydrolysed with water (150 ml), and extracted with $CHCl_3$, the combined organic layers washed with water and dried over $MgSO_4$. Evaporation gave a white powder corresponding to the N-alkylation products (1.16g, yield = 40%, **19/21**: 80/20). Several attempts of crystallisation did not increase the **19/21** ratio. **20** was similarly synthesized starting from (4-chloropropyl)dimethylchlorosilane (**12**, 2.16 ml, 12 mmol) with a prolonged reaction time (1 week) to afford a white powder corresponding to the N-alkylation products (yield = 60%, **20/22**: 80/20). Crystallisation from CH_2Cl_2/MeOH (50/50) afforded only one isomer: **20** (26%).

19 Rf: 0.35, dichloromethane/methanol: 90/10. IR and NMR analysis performed on **19/21** mixture revealed signals in accordance with the expected structure.

IR (KBr), ν_{max} cm^{-1}: 3300 and 3170 (NH_2), 3110 (C—H ar), 2910 (C—H aliphatic), 1680, 1600, 1580; 1250, 840 and 760 (Si—Me), 1100–1040 (br b, Si—O—Si).

^{1}H-NMR (DMSO-d_6): −0.06 (s, 6H, Me—Si), 0.35 (m, 2H, H3'), 1.74 (m, 2H, H2'), 4.09 (t, J = 6.7 Hz, 2H, H1'), 8.18 (s, 1H, H8 Ad), 8.19 (s, 1H, H2 Ad).

^{13}C-NMR (DMSO-d_6): 0.14 (Me—Si), 14.56 (C3'), 23.50 (C2'), 45.68 (C1'), 118.77 (C5), 140.91 (C8), 149.53 (C4), 152.34 (C2), 155.94 (C6)

^{29}Si-NMR (DMSO-d_6): 12.96.

MS, m/z (%): 484.2 (M+, 10), 335.9 (30), 308 (100), 234 (18), 149 (37).

20 mp: 171°C; Rf: 0.35, dichloromethane/methanol: 90/10

IR(KBr), ν_{max} cm^{-1}: 3300 and 3170 (NH_2), 3110 (C—H ar), 2910 (C—H aliphatic), 1680, 1600, 1580; 1250, 840 and 760 (Si—Me), 1100–1040 (br b, Si—O—Si).

^{1}H-NMR (DMSO-d_6): 0.01 (s, 6H, Me—Si), 0.55 (m, 2H, H4'), 1.29 (m, 2H, H3'), 1.89 (m, 2H, H2'), 4.23 (t, J: 7 Hz, 2H, H1'), 7.24 (2H, NH_2), 8.20 (s, 1H, H8 Ad), 8.22 (s, 1H, H2 Ad)

^{13}C-NMR (DMSO-d_6): 4.14 (Me—Si), 20.98 (C4'), 23.66 (C3'), 36.65 (C2'), 46.41 (C1'), 122.70 (C5), 144.71 (C8), 153.50 (C4), 156.22 (C2), 159.86 (C6).

MS, m/z (%): 512.1 (M+, 33), 497.2 (10), 378 (4), 322 (100), 190 (58), 149 (96), 135 (50)

Anal. Calcd. for $C_{22}H_{36}N_{10}OSi_2$: C, 51.53; H, 7.08; N, 27.31. Found: C, 51.53; H, 7.36; N, 26.92.

23 *1,3-Bis[3-(N-imidazolyl)propyl]-1,1,3,3-tetramethyldisiloxane.* To a solution of imidazole (2.04g,

30 mmol) in dry THF (50 ml) was slowly added NaH (0.70g, 97% in oil, 28.69 mmoles) and the mixture stirred for 80 mn at room temperature. 3-(chloropropyl)dimethylchlorosilane (**11**, 2.1 ml, 13 mmol) was then added, and the mixture refluxed for 4 days. The resulting solution was hydrolysed with water and extracted with CH_2Cl_2, the combined organic layers washed with water and dried over $MgSO_4$. After concentration under reduced pressure, the oily residue was applied to a silica gel column (CH_2Cl_2/MeOH: 95/5) to yield a clear oil (**23**, 1.34g, 59%); Rf: 0.53 dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3400 (br b, NH), 3100 (C—H olefinic), 2950–2900 (C—H aliphatic), 1650 (br b, C=N Imidazole), 1510 (C=C arom); 1250, 860 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.00 (s, 6H, Me—Si), 0.43 (m, 2H, H3'), 1.73 (m, 2H, H2'), 3.90 (t, J = 7 Hz, 2H, H1'), 6.88 (s, 1H, H4 or H5), 7.03 (s, 1H, H4 or H5), 7.47 (s, 1H, H2).

^{13}C-NMR ($CDCl_3$): −0.16 (Me—Si), 14.67 (C3'), 24.94 (C2'), 49.37 (C1'), 118.36 (C5), 128.94 (C4), 136.71 (C2)

MS, m/z (%): 350.1 (M+, 29), 269.1 (99), 241 (74), 216 (26), 183(6), 147 (18).

Anal. Calcd. for $C_{16}H_{30}N_4OSi_2$: C, 54.81; H, 8.62; N, 15.98. Found: C, 55.27; H, 8.73; N, 16.07.

24 *1,3-Bis[3-(N-indolyl)propyl]-1,1,3,3-tetramethyldisiloxane.* To a solution of indole (1.22g, 10.41 mmol) in dry DMSO (50 ml) was slowly added NaH (0.25g, 97% in oil, 9.94 mmoles) and the mixture stirred for 2 h at 50°C. 1,3-bis(3-chloropropyl)-1,1,3,3-tetramethyldisiloxane (**13**, 1.36g, 4.73 mmol) was then added, and the mixture heated 4 days at 100°C. The resulting solution was hydrolysed with water (200 ml), extracted with ether, the combined organic layers washed with water and dried over $MgSO_4$. After distillation of the unreacted starting material, the remaining oil was chromatographed over a silica gel column to yield **24** as an orange-colored oil (**24**, 0.57g, 27%); Rf: 0.75, dichloromethane.

IR (KBr), ν_{max} cm^{-1}: 3060 (C—H olefinic), 2950–1850 (C—H aliphatic), 1640 (wb, C=N conjugated), 1510 and 1450 (C=C ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.00 (s, 6H, Me—Si), 0.46 (m, 2H, H3'), 1.80 (m, 2H, H2'), 4.05 (t, J = 7 Hz, 2H, H1'), 7.10–7.65 (m, 6H, H ar).

^{13}C-NMR ($CDCl_3$): 0.0 (Me—Si), 15.5 (C3'), 24.7 (C2'), 49.5 (C1'), 101 (C3), 109.5 (C7), 119, 120.5, 121 (C4, C5, C6), 128 (C2), 128.5 (C3a), 136 (C7a)

MS, m/z (%): 448.1 (M+, 100), 433 (4), 290 (27), 247.9 (32.5), 231.9 (15), 129.9 (45).

Anal. Calcd. for $C_{26}H_{36}N_2OSi_2$: C, 69.59; H, 8.08; N, 6.24. Found: C, 69.51; H, 8.23; N, 6.39.

25 *1,3-Bis[3-(2-mercaptopyrimidinyl)propyl]-1,1,3,3-tetramethyldisiloxane.* To a solution of 2-mercaptopyrimidine (2.24g, 20 mmol) in dry DMSO (50 ml) was slowly added NaH (0.46g, 97% in oil, 19.13 mmol) and the mixture stirred 40 mn at 50°C. 3-(chloropropyl)dimethylchlorosilane (**11**, 1.43 ml, 8.69 mmol) was then added, and the mixture heated at 50°C for 3 days. The resulting solution was hydrolysed with water (200 ml) and extracted with CH_2Cl_2, the combined organic layers washed with water and dried over $MgSO_4$. The remaining oily residue was chromatographed over a silica gel column (CH_2Cl_2) to yield **25** as a clear oil, (0.89g, 47%); Rf: 0.65, dichloromethane.

IR (KBr), ν_{max} cm^{-1}: 3050 (C—H olefinic), 2950–2850 (C—H aliphatic), 1560 and 1540 (C=N, C=C ar), 1380; 1250, 840 and 760 (Si—Me); 1190 (C—S), 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.05 (s, 6H, Me—Si), 0.65 (m, 2H, H—C(3')), 1.72 (m, 2H, H—C(2')), 3.12 (t, J = 7 Hz, 2H, H—C(1')), 6.94 (dd, J = 5 Hz, 1H, H—C(3)), 8.49 (d, J = 5 Hz, 2H, H—C(2)).

^{13}C-NMR ($CDCl_3$): 0.05 (Me—Si), 17.68 (C3'), 23.11 (C2'), 34 (C1'), 116 (C3), 156.50 (C2), 172.1 (C1).

MS, mz (%): 439.1 (M+, 10), 424.1 (9), 326.1 (70), 285 (100), 242.9 (78), 210 (46), 173 (7), 133 (53).

Anal. Calcd. for $C_{18}H_{30}N_4OS_2Si_2$: C, 49.27; H, 6.89; N, 12.76. Found: C, 49.46; H, 7.17; N, 12.33.

26 *1,3-Bis[3-(5-chloro-2-mercaptobenzothiazolyl)propyl]-1,1,3,3-tetramethyldisiloxane.* To a solution of 5-chloromercaptobenzothiazole (1g, 5 mmol) in dry benzene (50 ml) was slowly added NaH (0.12g, 97% in oil, 4.78 mmol) and the mixture stirred at 90°C for 3 h. 3-(chloropropyl)dimethylchlorosilane (**11**, 0.36 ml, 2.17 mmol) was then added and the mixture heated 4 days under reflux, and the solvent removed under reduced pressure. The solid residue was hydrolysed with water (100 ml), extracted with CH_2Cl_2, the organic phase dried over $MgSO_4$, and concentrated to dryness. The resulting solid was applied to a silica gel column (hexane/CH_2Cl_2: 50/50) to yield **26** (0.14g, 21%); mp: 68°C; Rf: 0.82, dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3050 (C—H olefinic), 2970–2800 (C—H aliphatic), 1420 (ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.07 (s, 6H, Me—Si), 0.70 (m, 2H, H3′), 1.82 (m, 2H, H2′), 3.30 (t, J = 7 Hz, 2H, H1′), 7.22 (m, 1H, H7, Jab = 10 Hz), 7.62 (m, 1H, H6, Jab = 10 Hz), 7.81 (s, 1H, H4).

^{13}C-NMR ($CDCl_3$): 0.70 (Me—Si), 18 (C3′), 23.50 (C2′), 36.90 (C1′), 121, 121.50 and 124.50 (3C—H ar), 131.85, 133, 154 (3C quat ar), 169.50 (C2).

MS, m/z (%): 618 (M+, 1), 375 (10), 373.9 (34), 331.8 (28), 301 (44), 300.1 (36), 298.9 (100).

Anal. Calcd. for $C_{24}H_{30}Cl_2N_2OS_4Si_2$: C, 46.75; H, 4.91; N, 4.55. Found: C, 46.78; H, 5.05; N, 4.48.

General preparation of the 2-aminobenzamido compounds: **30** *1,3-bis[3-(2-aminobenzamido)propyl-1,1,3,3-tetramethyldisiloxane*; **34** *1,3-bis[3-(5-chloro-2-aminobenzamido)propyl]-1,1,3,3-tetramethyldisiloxane*; **36** *1,3-bis[3-(2-N-methylaminobenzamido)propyl]-1,1,3,3-tetramethyldisiloxane*. To a stirred suspension of isatoic anhydride (80 mmol) in absolute ethanol (160 ml) was added 1,3-bis(3-aminopropyl)-1,1,3,3-tetramethyldisiloxane (40 mmol). After stirring for 2 h at room temperature, the resulting mixture was poured into H_2O and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, evaporated and purified by chromatography over a silica gel column (CH_2Cl_2/MeOH: 90/10) to afford the desired compounds as white solids.

30 (18.75g, 96%); mp: 100°C; Rf: 0.75, dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3400 and 3300 (NH and NH_2), 3080 (C—H olefinic), 2980–2840 (C—H aliphatic), 1620 (C=O), 1590 and 1530 (C=C ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.08 (s, 6H, Me—Si), 0.55 (m, 2H, H3′), 1.62 (m, 2H, H2′), 3.35 (q, J = 7 Hz, 2H, H3′), 6.35 (br, 1H, N—H), 6.60 (m, 2H, H4, H6), 7.18–7.32 (m, 2H, H3, H5).

^{13}C-NMR ($CDCl_3$): 0.16 (M—Si), 15.36 (C3′), 23.44 (C2′), 42.34 (C1′), 116.49 (C3), 116.95 (C5), 127.12 (C6), 131.78 (C4), 148.30 (C2), 169.21 (C=O).

MS, m/z (%), 486.1 (26, M+), 308.9 (26), 235 (50), 499 (83), 120 (100), 114 (32), 92 (13).

Anal. Calcd. for $C_{24}H_{38}N_4O_3Si_2$: C, 59.22; H, 7.87; N, 11.51. Found: C, 58.99; H, 7.54; N, 11.74.

34 (1.29g, 74%); mp: 116°C; Rf: 0.80, dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3420 and 3300 (NH sec amide and NH_2), 3080 (C—H ar), 2980–2840 (C—H aliphatic), 1620 (C=O), 1590 and 1540 (C=C ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.06 (s, 6H, Me—Si), 0.55 (m, 2H, H3′), 1.61 (m, 2H, H2′), 3.35 (q, J = 7 Hz, 2H, H1′), 6.37 (br, 1H, NH), 6.58 (d, J = 8.7 Hz, 1H, H3), 7.09 (dd, J = 8.7 and 2.3 Hz, 1H, H4), 7.29 (d, J = 2.3 Hz, 1H, H6).

^{13}C-NMR ($CDCl_3$): 0.31 (Me—Si), 15.54 (C3′), 23.58 (C2′), 42.68 (C1′), 117.54 (C1), 118.37 (C3), 120.84 (C2), 126.79 (C6), 131.80 (C4) 146.95 (C5), 168.21 (C=O).

MS, m/z (%): 556.1 (M+, 13), 555.4 (6), 554 (16), 342.9 (31), 269.1 (64), 148.9 (100).

Anal. Calcd. for $C_{24}H_{36}Cl_2N_4O_3Si_2$: C, 51.88; H, 6.53; N, 10.08. Found: C, 51.90; H, 6.55; N, 10.02.

36 (8.11g, 64%); mp: 78°C; Rf: 0.95, dihloromethane/methanol: 90/10.
IR (KBr), ν_{max} cm^{-1}: 3400–3200 (NH and NH_2), 3080 (C—H ar), 2980–2770 (C—H aliphatic), 1620 (C=O), 1570 and 1510 (C=C ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.05 (s, 6H, Me—Si), 0.54 (m, 2H, H3′), 1.59 (m, 2H, H2′), 2.79 (s, 3H, N—Me), 3.34 (q, J = 7 Hz, 2H, H1′), 6.32 (br, 1H, N—H), 6.52 (td, J = 8.3 and <1 Hz, 1H, H5), 6.62 (d, J = 8 Hz, 1H, H3), 7.33 (m, 2H, H4, H6).

^{13}C-NMR ($CDCl_3$): 0.18 (Me—Si), 15.41 (C3′), 23.51 (C2′), 29.45 (N—Me), 42.39 (C1′), 110.78 (C3), 114.28 (C5), 115.34 (C1), 127.08 (C6), 132.40 (C4), 150.20 (C2), 169.72 (C=O).

MS, mz (%): 515.1 (M+, 38), 514.2 (100), 499.3 (3), 298.8 (51), 148.9 (71), 133.9 (100).

Anal. Calcd. for $C_{26}H_{42}N_4O_3Si_2$: C, 60.66; H, 8.22; N, 10.88. Found: C, 60.78; H, 8.08; N, 10.79.

31 *1,3-Bis[3-(4-oxo-N-3-quinazolinyl)propyl]-1,1,3,3-tetramethyldisiloxane* and **35** *1,3-bis[3-(4-oxo-6-chloro-N-3-quinazolinyl)propyl]-1,1,3,3-tetramethyldisiloxane*. A mixture of orthobenzamide **30** (1g, 2.05 mmol) and formic acid (1.6 ml, 4.20 mmol) was refluxed for 2 h, then poured into water (200 ml), and extracted with CH_2Cl_2. The organic layer was washed with water, dried over $MgSO_4$ and concentrated under

reduced pressure. The oily residue was applied to a silica gel column eluted with CH_2Cl_2 to yield **31** as a clear oil (0.97g, 95%).

Compound **35** was similarly synthesized starting from the chloro orthobenzamide (**34**, 2.77g, 5 mmol) with a prolonged reaction time (20 h reflux) which afforded **35** as an oil (1.70g, 60%).

31; Rf: 0.86, dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3100 (C—H ar), 2980–2840 (C—H aliphatic), 1680 (C=O), 1610 (C=N), 1560 and 1480 (ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.05 (s, 6H, Me—Si), 0.53 (m, 2H, H3'), 1.80 (m, 2H, H2'), 3.97 (t, J = 7 Hz, 2H, H1'), 7.49 (m, 1H), 7.72 (m, 2H), 8.30 (dd, J = 7.3 and <1 Hz, 1H), H5, H6, H7, H8, 8.1 (s, 1H, H2).

^{13}C-NMR ($CDCl_3$): 0.04 (Me—Si), 14.97 (C3'), 23.11 (C2'), 49.54 (C1'), 121.92 (C4a), 126.38, 126.87, 127.10, 133.81 (C5, C6, C7, C8), 146.5 (C2), 147.87 (C8a), 160.70 (C4).

MS, m/z (%): 506.1 (M+, 10), 491 (23), 318.9 (100), 276.9 (75), 244.7 (36), 132.8 (31).

Anal. Calcd. For $C_{26}H_{34}N_4O_3Si_2$: C, 61.63; H, 6.76; N, 11.06. Found: C, 61.60; H, 6.86; N, 10.94.

35 Rf: 0.84, dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3080 (C—H ar), 2980–2800 (C—H aliphatic), 1680 (C=O), 1610 and 1570 (C=C and C=N), 1480 (C=C), 1370; 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si), 645 (C—Cl).

^{1}H-NMR ($CDCl_3$): 0.00 (s, 6H, Me—Si), 0.51 (m, 2H, H3'), 1.75 (m, 2H, H2'), 3.93 (t, J = 7.3 Hz, 2H, H3'), 7.6 (m, 2H, H5, H8), 8.03 (s, 1H, H2), 8.21 (m, 1H, H7).

^{13}C-NMR ($CDCl_3$): 0.01 (Me—Si), 14.93 (C3'), 23.04 (C2'), 49.63 (C1'), 122.88 (C4a), 125.67, 128.76, 134.11 (C5, C7, C8), 132.53 (C8a), 146.31 (C8), 146.65 (C2), 159.59 (C4).

MS, m/z (%): 573.9 (3, M+), 559 (6), 353 (100), 310.9 (65), 279 (17), 162.9 (27).

32 *1,3-Bis[3-(4-oxo-N-3-(1,2-dihydroquinazolinyl))propyl]-1,1,3,3-tetramethyldisiloxane.* To a solution of quinazolinone **31** (1.31g, 2.63 mmol) in dry ether (40 ml) was slowly added $LiAlH_4$ (0.40g, 10.52 mmol). The resulting mixture was refluxed for 3 days, then hydrolysed with a saturated NH_4Cl solution, and extracted with ether. The organic layer was dried over $MgSO_4$, concentrated under reduced pressure and purified by chromatography over a silica gel column (CH_2Cl_2/MeOH: 95/5) to yield **32** as an oil (1.68g, 90%); Rf: 0.72, dichloromethane/methanol: 90/10.

IR (KBr) ν_{max} cm^{-1}: 3300 (NH sec), 3050 (C—H arom), 2950–2700 (C—H aliphatic), 1640 (br b, C=O), 1580 and 1490 (ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.02 (s, 6H, Me—Si), 0.52 (m, 2H, H3'), 1.60 (m, 2H, H2'), 3.47 (t, J = 7 Hz, 2H, H1'), 4.48 (2s, 2H, H2), 4.63 (s, 1H, NH), 6.65 (d, 1H, H8), 6.83 (dd, 1H, H6), 7.25 (ddd, 1H, H7), 7.89 (dd, 1H, H5), J5,6 = 9.1 Hz, J5,7 = 1.5 Hz, J6,7 = 6.8 Hz, J5,8 = 0.3 Hz, J6,8 = 1.1 Hz, J7,8 = 7.7 Hz coupling constants determined by modelisation.

^{13}C-NMR ($CDCl_3$): 0.30 (C1), 15.42 (C2), 21.68 (C3), 48.05 (C4), 59.43 (C12), 114.77 (C10), 117.51 (C6), 119.41 (C8), 128.62 (C7), 132.93 (C9), 147.76 (C11), 163.58 (C5).

MS, m/z (%): 510.78 (M+, 2), 508.2 (7), 495 (3), 321.1 (26), 319 (83), 247.1 (56), 245 (100), 146.9 (72), 132 (37).

Anal. Calcd. for $C_{26}H_{34}N_4O_3Si_2$: C, 61.18; H, 7.49; N, 10.96. Found: C, 60.49; H, 7.56; N, 11.01.

33 *1,3-Bis[3-(N-3(1,2,3,4-tetrahydroquinazolinyl))propyl]-1,1,3,3-tetramethyldisiloxane.* To a solution of quinazolinone (**32**, 1.08g, 2.17 mmol) in dry ether (40 ml) was slowly added $LiAlH_4$ (0.33g, 8.70 mmol). The resulting mixture was refluxed for 6 days, then hydrolysed with a saturated NH_4Cl solution, and extracted with ether. The organic layer was dried over $MgSO_4$, concentrated under reduced pressure and purified by chromatography over a silica gel column (CH_2Cl_2/MeOH: 95/5) to yield **33** as an oil (50mg, 7%); Rf: 0.56, dichloromethane/methanol: 90/10.

IR (KBr), ν_{max} cm^{-1}: 3330 (NH), 3080 (C—H ar), 2960–2820 (C—H aliphatic), 1600 and 1490 (ar); 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.03 (s, 6H, Me—Si), 0.50 (m, 2H, H3'), 1.56 (m, 2H, H2'), 2.48 (t, J = 7.3 Hz, 2H, H1'), 3.81 (s, 2H, H4), 4.02 (s, 2H, H2), 6.52 (dd, 1H, H5), 6.67 (dt, 1H, H7), 6.89 (dd, 1H, H8), 7.0 (ddd, 1H, H6), J5,6 = 7.5 Hz, J5,7 = 1.3 Hz, J6,7 = 6.9 Hz, J5,8 = 0.0 Hz, J6,8 = 1.3 Hz, J7,8 = 6.9 Hz, coupling constants determined by modelisation.

^{13}C-NMR ($CDCl_3$): 0.30 (C1), 15.83 (C2), 21.51 (C3), 53.56 (C4), 56.30 (C5), 63.33 (C12), 115.15 (C10), 118.17 (C8), 120.15 (C6), 127.08 and 127.40 (C9 and C7), 142.67 (C11).

MS, m/z (%): 482.1 (M+, 58), 375.9 (100), 362 (82), 146.9 (63), 133 (42), 118 (55).

Anal. Calcd. for $C_{26}H_{42}N_4OSi_2$: C, 64.68; H, 7.77; N, 11.60. Found: C, 65.21; H, 8.67; N, 10.98.

37 *1,3-Bis[3-(N-1-methyl-1,2-dihydroquinazolin-4-onyl))propyl]-1,3,3-tetramethyldisiloxane*. Paraformaldehyde (0.42g, 14.14 mmol) was added to a solution of the benzamide (**36**, 1.82g, 3.53 mmol) in toluene (100 ml). After refluxing for 5 h, the mixture was poured into water and extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$, evaporated and purified by chromatography over a silica gel column (CH_2Cl_2/MeOH: 95/5) to yield **37** as an oil (1.68g, 90%); Rf: 0.66, dichloromethane/methanol: 95/5.

IR (KBr), ν_{max}: 3080 (C—H ar), 2980–2770 (C—H aliphatic), 1660 (C=O cyclic amide), 1610, 1500 and 1480 (ar), 1380; 1250, 840 and 760 (Si—Me); 1100–1000 (br b, Si—O—Si).

^{1}H-NMR ($CDCl_3$): 0.05 (s, 6H, Me—Si), 0.53 (m, 2H, H3'), 1.60 (m, 2H, H2'), 2.85 (s, 3H, H_3C—N), 3.48 (t, 2H, H1'), 4.38 (s, 2H, H2), 6.66 (d, J = 8.1 Hz, 1H, H8), 6.87 (dt, J = 7.4 and <1 Hz, 1H, H6), 7.36 (ddd, J = 8.1, 7.4 and 1.5 Hz, 1H, H7), 7.95 (dd, J = 7.7 and 1.5 Hz, 1H, H5).

^{13}C-NMR ($CDCl_3$): 0.26 (C1), 15.37 (C2), 21.58 (C3), 35.85 (C12), 48.29 (C4), 66.64 (C13), 111.90 (C10), 117.96 (C6), 118.88 (C8), 128.77 (C7), 133.10 (C9), 149.11 (C11), 163.09 (C5).

MS, m/z (%): 538.1 (M+, 2), 523.1 (4), 335 (6), 277 (27), 261.1 (39), 161 (100).

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