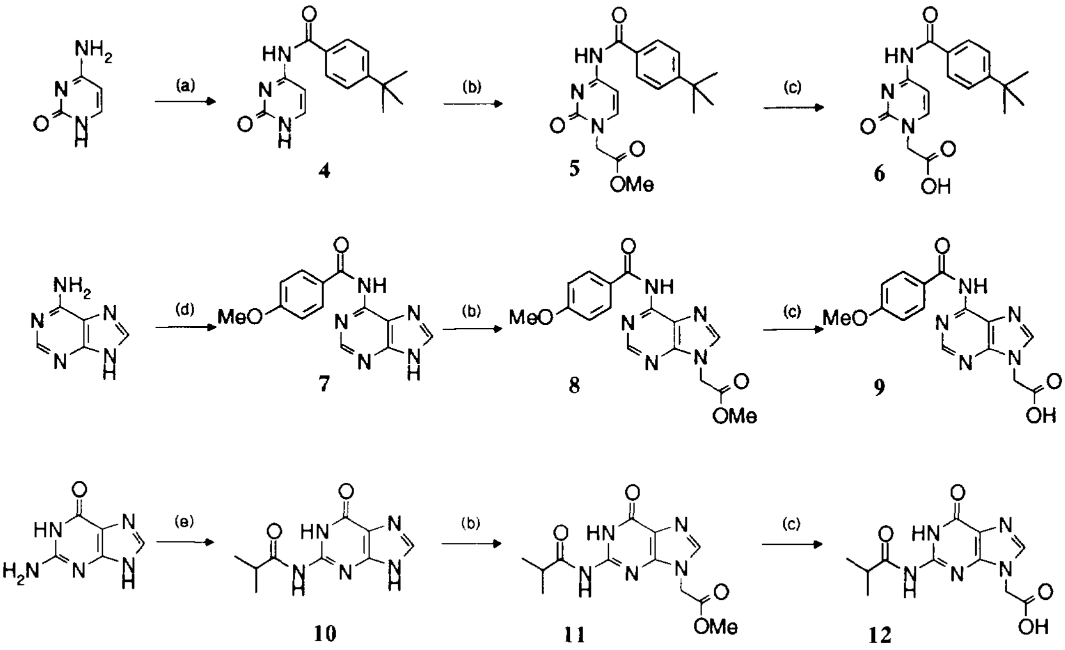
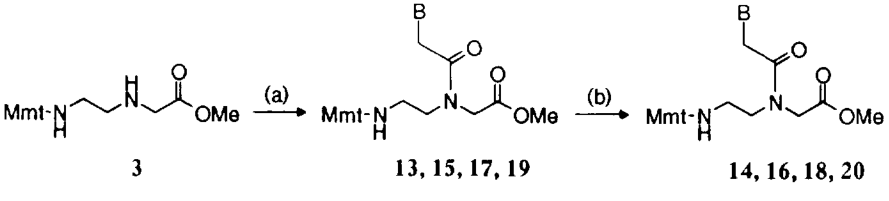


Reagents and Conditions: (a) *tert*-Butylbenzoyl chloride, NEt_3/ DMF; (b) Methyl bromoacetate, NaH/ DMF; (c) NaOH, H_2O/ dioxane; (d) Anisoyl chloride/ pyridine; (e) Isobutanoyl chloride, NEt_3/ DMF.

Scheme 2: Synthesis of acyl-protected carboxymethyl nucleobases.

Adenine was protected by heating with anisoyl chloride in pyridine. The resulting N^6-anisoyladenine **7** was alkylated to give **8**, and saponified to give **9** using procedures analogous to those used for the preparation of **6**. N^2-Isobutanoyl guanine **10** was synthesized by heating guanine with isobutanoyl chloride in DMF and triethylamine. This was then alkylated using NaH / methyl bromoacetate to give the desired N^9-alkylated derivative **11** along with other regioisomers which could be separated by column chromatography. Saponification using aqueous NaOH gave the free acid **12**.



13 and **14**, B= thymine; **15** and **16**, B= N^4-*t*-butylbenzoyl cytosine
17 and **18**, B= N^6-anisoyl adenine; **19** and **20**, B= N^2-isobutanoyl guanine

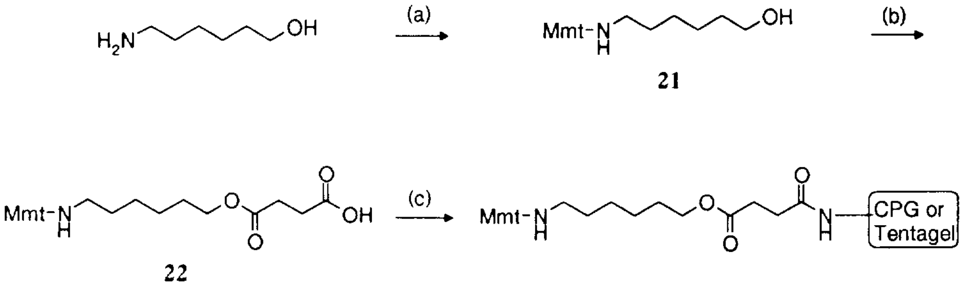
Reagents and Conditions: (a) Carboxymethyl nucleobase, DIPC, HOOBt, NEM/ DMF;
(b) NaOH, H_2O/ dioxane

Scheme 3: Synthesis of Mmt-protected PNA monomers.

The carboxymethylated nucleobases were coupled to the Mmt-(2-aminoethyl)glycine methyl ester backbone unit **3** using diisopropylcarbodiimide (DIPC) in DMF in the presence of HOOBt and N-ethylmorpholine. Saponification of the resulting methyl esters **13**, **15**, **17** and **19** under controlled conditions gave the desired acyl-protected PNA monomers **14**, **16**, **18** and **20** (Scheme 3).

The Solid Support

Standard peptide synthesis solid supports require treatment with strong acid to cleave the peptide chain from the support. These conditions are incompatible with our orthogonal protecting group strategy and would not allow a combination of PNA and oligonucleotide synthesis. Therefore we synthesized universal solid supports which are cleavable during the ammonia treatment used for base-deprotection, and are therefore compatible with the new synthetic strategy (Scheme 4). These supports utilise an aminohexyl spacer and a base-cleavable succinyl linker. Thus 6-aminohexan-1-ol was selectively N-tritylated using Mmt chloride in pyridine to give **21**. The resulting alcohol was succinylated using succinic anhydride and DMAP in pyridine to give **22**. This was then coupled to AminoTentagel™ or Aminopropyl CPG (Controlled-Pore Glass) using TBTU / N-ethylmorpholine in DMF. PNAs are obtained after synthesis and ammonia cleavage as their C-terminal hydroxyhexylcarboxamides.



Reagents and Conditions: (a) MmtCl/ pyridine; (b) Succinic anhydride, DMAP/ pyridine; (c) Aminopropyl CPG or Amino-Tentagel, TBTU, N-ethylmorpholine/ DMF.

Scheme 4: Synthesis of Universal Solid Support for PNA Synthesis.

Solid-phase Synthesis

The monomers were used, in conjunction with the CPG or Tentagel™ solid-supports described above, for the synthesis of PNAs on a modified Eppendorf Biotronik Ecosyn™ D-300 DNA synthesizer. PNAs were synthesized on a 5-10µmol scale. These small scale syntheses produce ample material for *in vitro* screening for biological activity. Deprotection of the Mmt group occurs by treatment with 3% trichloroacetic acid in CH_2Cl_2. Excess acid is removed by subsequent washing with acetonitrile and 0.3M N-ethylmorpholine or N,N-diisopropyl-N-ethylamine in DMF. For coupling the monomer (0.3M solutions in DMF) is activated by PyBOP or HATU (0.3M solution in DMF) in the presence of N-ethylmorpholine (0.3M solution in DMF). For this, the reagents are pre-mixed in the delivery syringe of the synthesizer and, after a short preactivation period, delivered to the reaction vessel. After 30 minutes of coupling, unreacted amino functions are capped using a mixture of acetic anhydride/N-methyl imidazole in THF, which is used as capping reagent in standard DNA synthesis.

Coupling efficiencies, determined by measurement of the Mmt cation released during deprotection, are generally in the range of 95 to 99%. After synthesis is completed, the PNA is cleaved from the solid-support and deprotected with conc. aqueous ammonia solution. The cleavage and deprotection sequence: treatment with conc. aqueous ammonia, followed by 80% aqueous acetic acid for removal of the N-terminal Mmt group prevents the diketo piperazine cleavage reaction reported previously.[8] The terminal Mmt protecting group can be left on if desired for 'Trityl-On' HPLC purification. *Figure 1* (A) shows the HPLC trace of crude 12mer PNA sequence H_2N-aca tca tgg tcg-(hex) on a reversed phase LiChrospher™ WP300 RP-18(e) column after detritylation. The crude, 'Trityl-Off' 12mer PNA was characterized by positive ion Electrospray mass spectrometry (*Figure 1,* C). The PNA was purified by HPLC using a RP-18 column and an acetonitrile gradient (2-7%) in 0.1% TFA in water. Following desalting by gel filtration, the PNA appears as a single peak on HPLC (*Figure 1,* B).

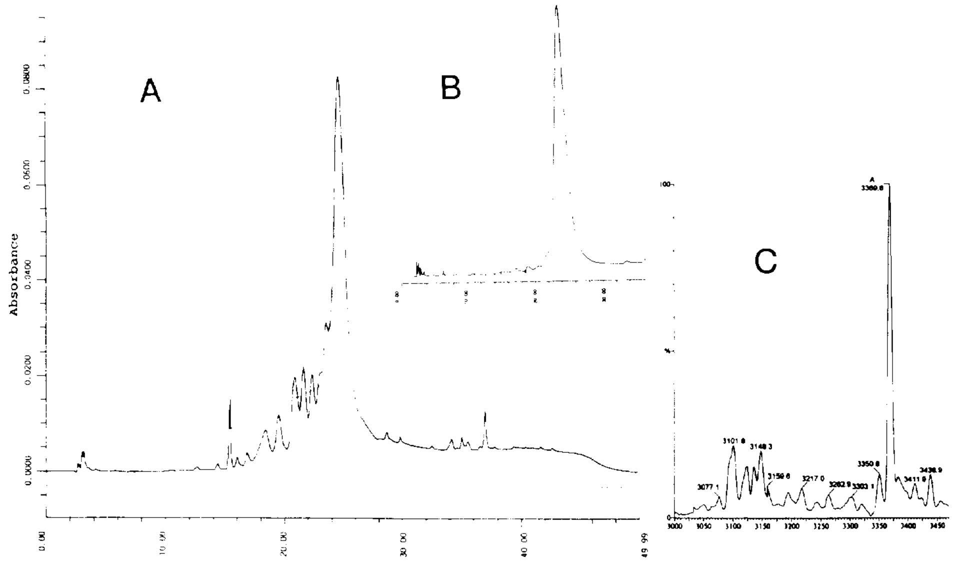


Figure 1: Reversed-phase HPLC trace and ES-MS spectrum of PNA sequence H_2N-aca tca tgg tcg-(hex). M(calculated) for $C_{135}H_{174}N_{70}O_{37}$ = 3369.31; M(experimental)=3369.6

In conclusion, we have described the synthesis of novel Mmt protected PNA monomers, and have demonstrated that the Mmt strategy works well for the synthesis of PNAs of mixed base composition. We routinely use the Mmt strategy for the synthesis of PNAs. This synthesis strategy is milder than both the Boc- and the Fmoc-strategy. In addition the synthesis and deprotection conditions are completely compatible with oligonucleotide synthesis, and we have used this synthetic strategy for the solid-phase synthesis of PNA-DNA chimeric oligomers (manuscript in preparation).

EXPERIMENTAL

General

The following abbreviations are employed: N,N'-diisopropylcarbodiimide (DIPC); 4,4-dimethylaminopyridine (DMAP); N,N-dimethylformamide (DMF); 3,4-dihydro-3-hydroxy-4-oxo-1,2,3-benzotriazine (HOOBt); O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium-hexafluorophosphate (HATU); 4-ethylmorpholine (NEM); O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium-tetrafluoroborate (TBTU); (benzotriazol-1-yloxy)-tripyrrolidinophosphonium-hexafluorophosphate (PyBOP).

The peptide coupling reagent HATU was purchased from Millipore (Eschborn, Germany); DNA/PNA synthesis reagents were purchased from MWG Biotech GmbH (Ebersberg, Germany); Tentagel™ was purchased from Rapp Polymers (Tübingen, Germany); all other reagents were obtained from Sigma-Aldrich-Fluka (Neu-Ulm, Germany). Flash chromatography was performed using Merck silica gel 60 (230-400mesh ASTM). TLC was carried out on Merck DC Kieselgel 60 F-254 glass plates. ^{1}H NMR was recorded in the solvents indicated at 270 Mhz. Chemical shifts (δ) are reported in parts per million down field relative to the internal TMS standard. Mass spectra were recorded using either Fast Atom Bombardment (FAB), Electrospray (ES) or Direct Chemical (DCI) ionisation. PNA synthesis was carried out on a modified Eppendorf Biotronik Ecosyn™ D-300 DNA synthesizer (Eppendorf Biotronik, Maintal, Germany). HPLC analysis of PNAs was carried out on a Beckman System Gold HPLC system using a LiChrospher™ WP300 RP-18(e) analytical column (4x250mm; E. Merck, Darmstadt; Germany), eluting with a linear gradient of eluent B in eluent A (A: 0.1% TFA in water; B: 0.1% TFA in 20% acetonitrile in water).

N-(2-Aminoethyl)glycine (1). 1,2-Diaminoethane (1.80l; 26.8mol) was dissolved in methanol (2.61l), and a solution of of glyoxylic acid monohydrate (840g; 9.13mol) in water (2.61l) was then added slowly while cooling and stirring. **Caution: Exothermic reaction**. Palladium (5%) on charcoal (78g) was then added to the mixture and hydrogenation was carried out in a hydrogenation vessel at 0.3 bar and at room temperature. After 200l of hydrogen had been taken up, the reaction was complete and the catalyst was filtered off. The filtrate was concentrated *in vacuo* and the residue was subsequently distilled twice together with toluene; methanol (1.56l) was added to the residue and the mixture was stirred thoroughly at approximately 0° C. The precipitate was filtered off, then washed with methanol. A second crop was obtained from the mother liquor after concentration. The combined product was dried *in vacuo* to give **1** as a white solid in 588g (55%) yield. M.p. 149-153°C(dec.); R_f (n-butanol:acetic acid:water:ethyl acetate/1:1:1:1) 0.2; MS(DCI) 119 $[M+H]^+$; ^{1}H NMR (D_2O) δ 3.35 (2H, s, CH_2-CO); 2.92-3.18 (4H, m, CH_2-CH_2).

Methyl N-(2-aminoethyl) glycinate dihydrochloride (2). Compound 1 (460g; 3.9mol) was suspended in methanol (14.0l), and HCl gas (500g) was passed into the suspension. **Caution: Exothermic reaction.** The mixture became hot and was then maintained under reflux for a total of 8h. The mixture was cooled to 0° C and stirred at this temperature for 3h. The product was filtered off and dried *in vacuo* to give **2** as colorless crystals in 716g (90%) yield . M.p. 190-192°C. R_f (n-butanol:acetic acid:water:ethyl acetate/1:1:1:1) 0.3; MS(DCl) 133 $[M+H]^+$; ^1H NMR (D_2O) δ 4.18 (2H, s, CH_2-CO); 3.92 (3H, s, CO-OCH_3); 3.42-3.65 (4H, m, CH_2-CH_2).

Methyl N-[2-((4-methoxyphenyl)-diphenylmethyl)aminoethyl] glycinate (3). Compound 2 (14.8g; 72.2mmol) was suspended in DMF (300ml) and the suspension was treated with triethylamine (30.2ml; 220mmol), with stirring. The mixture was cooled to approximately 4°C, and a solution of Mmt-Cl (22.2g; 72.2mmol) in CH_2Cl_2 (100ml) was added dropwise, with vigorous stirring. Stirring was continued for 2.5h at room temperature. Precipitated triethylammonium hydrochloride was then filtered off, ethanol (10ml) was added to the solution, and the filtrate was concentrated *in vacuo*. The residue was then chromatographed on silica gel using a mixture of diethyl ether:petroleum ether:triethylamine/ 200:100:3. The product-containing fractions were combined and evaporated to dryness *in vacuo* to give **3** as an oil which crystallizes slowly upon standing in 18.8g (65%) yield. R_f =0.16 (diethyl ether:petroleum ether/ 2:1 + 1% triethylamine); MS(FAB/MeOH/NBA/LiCl) 411.2 $[M+Li]^+$; ^1H NMR ($CDCl_3$) δ 7.50-6.80 (14H, m, Mmt); 4.80 (3H, s, Mmt-OMe); 4.70 (3H, s, COOMe); 3.35 (2H, s, glycine-CH_2); 2.70 (2H, t, CH_2-1); 2.25 (2H, t, CH_2-2); 1.80 (2H, br s, NH).

N^4-(4-*tert*-Butylbenzoyl)cytosine (4). Cytosine (11.1g; 0.10mol) was suspended in dry DMF (250 ml), and triethylamine (15.4 ml; 0.11mol) was added. 4-*tert*-butylbenzoyl chloride (18.6 ml; 0.10mol) was added dropwise using a syringe. Stirring was continued for 4h at room temperature and more 4-*tert*-butylbenzoyl chloride (3.7 ml; 0.02mol) was then added. After a further 2h, the reaction was quenched by the addition of a small amount of methanol. The solvent was removed *in vacuo*, and the residue was treated with CH_2Cl_2 and water. The resulting precipitate was filtered off and dried *in vacuo* to give **4** as a white solid in 15.7g (61%) yield. R_f = 0.55 (CH_2Cl_2:MeOH/9:1); MS(DCI) 272 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 11.30 (2H, br s, NH); 8.00 (2H, d, tBuBz H-2 and 6); 7.85 (1H, d, cytosine H-6); 7.50 (2H, d, tBuBz H-3 and 5); 7.20 (1H, d, cytosine H-5); 1.30 (9H, s, tBu).

1-(Methoxycarbonylmethyl)- N^4-(4-*tert*-butylbenzoyl)cytosine (5). Compound 4 (15.0g; 55.3mmol) was suspended in dry DMF (250 ml), sodium hydride (1.32 g; 55.0mmol) was added in portions, and the mixture was stirred for 1h at room temperature. Methyl bromoacetate (5.20 ml; 56.0mmol) was added dropwise at room temperature using a syringe. Stirring was continued for 1h at room temperature, and methanol (10 ml) was then added. The solvent was removed *in vacuo*, and the residue was partitioned between CH_2Cl_2 and water. The organic phase was washed with water, dried (Na_2SO_4), filtered and evaporated *in vacuo*. The resulting crude product was recrystallized from isopropanol to give **5** as a white solid in 8.00g (42%) yield. M.p.: 189-193°C (dec.); R_f = 0.72 (CH_2Cl_2:MeOH/9:1); MS(DCI) 344 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ 8.70 (1H, br s, NH); 7.80 (2H, d, tBuBz H-2 and 6); 7.55 (4H, m, cytosine H-5,6; tBuBz H-3 and 5); 4.65 (2H, s, CH_2); 3.80 (3H, s, OMe); 1.30 (9H, s, tBu).

1-(Carboxymethyl)- N^4-(4-*tert*-butylbenzoyl)cytosine (6). Compound 5 (8.0g; 24mmol) was dissolved in a mixture of dioxane (50ml) and water (10ml), and 2N aqueous sodium hydroxide solution was added dropwise with stirring at room temperature (pH 11-12). When hydrolysis of the methyl ester was complete, the pH of the reaction solution was brought to 3 using 2M $KHSO_4$ solution. The precipitate which separated out was filtered off. This crude product was dissolved in aqueous $NaHCO_3$ solution and reprecipitated by adding 2M

$KHSO_4$ solution. The product was filtered off, washed with a small amount of water and dried *in vacuo* to give **6** as a white solid in 6.62g (86%) yield. M.p. 285°C (dec); R_f = 0.2 (CH_2Cl_2:MeOH/9:1); MS(DCI) 330 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 8.10 (1H, d, cytosine H-6); 7.95 (2H, d, tBuBz H-2 and 6); 7.55 (2H, d, tBuBz H-3 and 5); 7.30 (1H,d, cytosine H-5); 4.55 (2H, s, CH_2); 1.30 (9H, s, tBu).

***N^6*-(4-Methoxybenzoyl)adenine (7).** Adenine (13.5g; 0.10mol) was suspended in dry pyridine (250 ml). 4-Methoxybenzoyl chloride (17.1g; 0.10mol) was added dropwise using a syringe. The mixture was stirred for 3h at 100°C and allowed to stand overnight at room temperature. The reaction solution was treated with methanol, and the solvent was subsequently evaporated *in vacuo*. The residue was coevaporated twice with toluene and then stirred with hot isopropanol. The mixture was allowed to cool slowly, and the product which precipitated out was filtered off and dried *in vacuo* to give **7** in 22.2g (82%) yield. M.p. 212-214°C; R_f = 0.67 (CH_2Cl_2:isopropanol/8:2); MS(+ES) 270 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 11.60 (1H, br s, NH); 9.00 (1H, br s, NH); 8.75 (1H, s, adenine H-2); 8.50 (1H, s, adenine H-8); 8.15 (2H, d, Anis H-2 and 6); 7.10 (2H, d, Anis H-3 and 5); 3.90 (3H, s, Anis-OMe).

***N^6*-(4-Methoxybenzoyl)-9-(methoxycarbonylmethyl)adenine (8).** Compound **7** (8.01g; 29.7mmol) was suspended in dry DMF (150 ml), sodium hydride (0.75g; 31.2mmol) was added in portions, and the mixture was stirred at room temperature for 30 min. Methyl bromoacetate (2.85ml; 30.9mmol) was added dropwise at room temperature using a syringe. Stirring was continued for 2h at room temperature, and the mixture was treated with a small amount of carbon dioxide in methanol. The solvent was evaporated *in vacuo*, the residue was dissolved in CH_2Cl_2 and washed once with water. The product precipitated from the organic phase and was filtered off. The filter residue was washed with a small amount of water and then dried *in vacuo* to give **8** as a white solid in 4.03g (40%) yield. R_f = 0.76 (ethyl acetate:MeOH/8:2); MS(+ES) 342 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ 9.00 (1H, br s, NH); 8.75 (1H, s, adenine H-2); 8.10 (1H, s, adenine H-8); 8.00 (2H, d, Anis H-2 and 6); 7.00 (2H, d, Anis H-3 and 5); 5.05 (2H, s, CH_2); 3.95 (3H, s, COOMe); 3.85 (3H, s, Anis-OMe).

***N^6*-(4-Methoxybenzoyl)-9-(carboxymethyl)adenine (9).** Compound **8** (1.71g; 5mmol) was suspended in water (40 ml), and 2N aqueous sodium hydroxide solution was added dropwise at 0°C while maintaining pH 11, until the methyl ester was completely hydrolysed. The reaction solution was filtered, and the pH of the filtrate was brought to 3 using 2M $KHSO_4$ solution, causing precipitation of the product. The precipitate was filtered off, washed with a small amount of cold water and dried *in vacuo* to give **9** as a white solid in 1.52g (93%) yield. M.p. 222-223°C (dec.) ; R_f = 0.2 (n-butanol:acetic acid:water/ 3:1:1); MS(+ES) 328 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 11.00 (1H, br s, NH); 8.70 (1H, s, adenine H-2); 8.45 (1H, s, adenine H-8); 8.05 (2H, d, Anis H-2 and 6); 7.10 (2H, d, Anis H-3 and 5); 5.10 (2H, s, CH_2); 3.90 (3H, s, Anis-OMe).

***N^2*-(Isobutanoyl)guanine (10).** Guanine (3.02g; 20mmol) was suspended in anhydrous DMF (40 ml), and triethylamine (1.45 ml; 10.4mmol) was added. Isobutanoyl chloride (2.12 g; 19.9mmol) was then added dropwise using a syringe. The mixture was stirred for 3h at 100°C. The reaction solution was then treated with methanol, and the solvent was subsequently evaporated *in vacuo*. The residue was stirred with hot isopropanol, and the precipitated product was filtered off and dried *in vacuo* to give **10** in 2.67g (60%) yield. R_f = 0.45 (n-butanol:acetic acid:water/ 3:1:1); MS (+ES) 222.2 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 12.05 (1H, br s, NH); 11.50 (1H, s, NH); 8.10 (1H, s, guanine H-8); 2.75 (1H, septet, iBu-CH); 1.10 (6H, d, iBu-CH_3).

***N^2*-(Isobutanoyl)-9-(methoxycarbonylmethyl)guanine (11).** Compound **10** (4.42g; 20mmol) was suspended in dry DMF (50 ml). Sodium hydride (0.5g; 20.8mmol) was added in portions, and the mixture was stirred for 1h at room temperature. Methyl bromoacetate (1.9 ml; 20.6mmol) was subsequently added dropwise at room temperature with a syringe. Stirring was continued for 1h at room temperature and the mixture was then treated with a small amount of carbon dioxide in methanol. The solvent was evaporated *in vacuo*, and the residue was purified by column chromatography on silica gel using CH_2Cl_2:methanol/95:5 as the eluent. The product-containing fractions were combined and concentrated *in vacuo* to give **11** as a white solid in 2.35g (40%) yield. R_f = 0.58 (CH_2Cl_2:MeOH/9:1); MS(DCI) 294 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ 12.25 (1H, br s, NH); 10.00 (1H, s, NH); 7.80 (1H, s, guanine H-8); 5.20 (2H, s, CH_2); 3.80 (3H, s, OCH_3); 2.80 (1H, septet, iBu-CH); 1.25 (6H, d, iBu-CH_3).

N^2-(Isobutanoyl)-9-(carboxymethyl)guanine (12). Compound **11** (19.7g; 67mmol) was suspended in water (100 ml), and 2N aqueous sodium hydroxide solution was added dropwise at 0°C while maintaining pH 11, until the methyl ester was completely hydrolysed. The reaction solution was then filtered, the pH of the filtrate was brought to 3 using 2M $KHSO_4$ solution, and the mixture was extracted using ethyl acetate. The aqueous phase was concentrated *in vacuo* to a volume of approximately 20 ml and covered with a layer of ethyl acetate. The precipitate which separated out slowly was filtered off and dried *in vacuo* to give **12** as a white solid in 11.57g (62%) yield. R_f = 0.34 (n-butanol:acetic acid:water/3:1:1); MS(+ES) 342 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 12.05 (1H, s, NH); 11.65 (1H, s, NH); 7.95 (1H, s, guanine H-8); 4.85 (2H, s, CH_2); 2.75 (1H, septet, iBu-CH); 1.10 (6H, d, iBu-CH_3).

Methyl N-[2-((4-methoxyphenyl)-diphenylmethylamino)-ethyl]-N-((thymin-1-yl)acetyl) glycinate (13). Compound 3 (1.00g; 2.48mmol) was dissolved in DMF (5ml). To this solution was added HOOBt (0.404g; 2.48mmol) and NEM (0.572g; 0.632ml; 4.96mmol). A solution of N-1-carboxymethylthymine (0.456g; 2.48mmol) in DMF (5ml) was then added, followed by DIPC (0.376g; 0.46ml; 3.0mmol). The reaction mixture was stirred for 20h at room temperature. The solvent was evaporated *in vacuo*, and the residue was dissolved in ethyl acetate. This solution was washed twice with water and once with saturated aqueous KCl solution. The organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The residue was applied to a silica gel chromatography column which had been equilibrated with CH_2Cl_2 containing 1% methanol and 1% triethylamine, and eluted with a gradient of 1-5% methanol in CH_2Cl_2. On concentration of the combined fractions containing the desired product a white precipitate of N,N'-diisopropylurea formed which was removed by filtration. **13** was obtained as a white foam in 1.28g (91%) yield. R_f =0.28 (CH_2Cl_2:MeOH/95:5); MS (FAB/MeOH/NBA) 571.2 $[M+H]^+$; ^1H NMR (d6-DMSO) δ 11.4 (1H, s, thymine H-3); 7.45-6.85 (15H, m, Mmt and thymine H-6); 4.82 and 4.55 (2H, 2xs {rotamers}, N-CO-CH_2); 4.45 and 4.02 (2H, 2xs {rotamers}, N-CH_2-CO_2Me); 3.85 (3H, s, Mmt-OMe); 3.58 (3H, s, COOMe); 3.45 (2H, m, CH_2-N); 2.15 (2H, m, MmtNH-CH_2); 1.75 (3H, s, thymine H-5).

N-[2-((4-Methoxyphenyl)-diphenylmethylamino)ethyl]-N-((thymin-1-yl)acetyl) glycine (14). Compound **13** (1.28g; 2.25mmol) was dissolved in dioxane (10ml) and water (2ml). The solution was cooled to 0°C and 1M aqueous NaOH was added dropwise until the solution reached pH11. After 2h the solution was adjusted to pH5 by the dropwise addition of 2M aqueous $KHSO_4$. The product was extracted into ethyl acetate, and the aqueous phase was extracted 3 times with ethyl acetate. The combined organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The residue was applied to a silica gel chromatography column and eluted with a gradient of 5-10% methanol and 1% triethylamine in CH_2Cl_2. The combined fractions containing the desired product were dried *in vacuo*, and coevaporated twice with pyridine and three times with toluene to remove excess triethylamine. **14** was obtained as a white foam in 1.07g (85%) yield. R_f =0.28 (CH_2Cl_2:MeOH/8:2). MS(FAB): 557.2402 ($C_{31}H_{32}N_4O_6$ + H requires 557.2400); ^1H NMR (d6-DMSO) δ 11.4

(1H, d, thymine H-3); 7.42-6.85 (15H, m, Mmt and thymine H-6); 4.82 and 4.48 (2H, 2xs {rotamers}, N-CO-CH_2); 3.95 and 3.80 (2H, 2xs {rotamers}, N-CH_2-CO_2H); 3.72 (3H, s, Mmt-OMe); 3.40 (2H, m, CH_2-N); 2.15 (2H, m, MmtNH-CH_2); 1.75 (3H, d, thymine H-5).

Methyl N-[2-((4-methoxyphenyl)-diphenylmethylamino)ethyl]-N-[(N^4-(4-*tert*-butylbenzoyl)-cytosin-1-yl) acetyl] glycinate (15). Compound 3 (1.00g; 2.48mmol) was dissolved in DMF (5ml). To this solution was added HOOBt (0.403g; 2.48mmol) and NEM (0.63ml; 4.96mmol). A suspension of 6 (0.740g; 2.48mmol) in DMF (5ml) was then added, followed by DIPC (0.47ml; 2.97mmol). The reaction mixture was stirred for 20h at room temperature. The solvent was evaporated *in vacuo*, and the residue was dissolved in ethyl acetate. This solution was washed twice with water and once with saturated aqueous KCl solution. The organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The residue was applied to a silica gel chromatography column which had been equilibrated with CH_2Cl_2:ethyl acetate/1:1, + 1% triethylamine, and eluted with CH_2Cl_2:ethyl acetate/1:1. On concentration of the combined fractions containing the desired product a white precipitate of N,N'-diisopropylurea formed which was removed by filtration. **15** was obtained as a pale yellow-white foam in 1.64g (92%) yield. R_f =0.31 (CH_2Cl_2:ethyl acetate/1:1). MS (FAB/MeOH/NBA/LiCl) 722.5 $[M+Li]^+$; ^1H NMR (d6-DMSO) δ 11.1 (1H, s, cytosine H-4); 8.00 (3H, m, 2xtBuBz H, cytosine H-6); 7.55 (2H, d, tBuBz H-3 and 5); 7.50-6.85 (15H, m, Mmt, cytosine H-5); 5.00 and 4.70 (2H, 2xs {rotamers}, N-CO-CH_2); 4.50 and 4.05 (2H, 2xs {rotamers}, N-CH_2-CO_2H); 3.75 (3H, s, Mmt-OMe); 3.58 (3H, s, COOMe); 3.40-3.50 (2H, m, CH_2-N); 2.20 (2H, m, MmtNH-CH_2); 1.35 (9H, s, tBu).

N-[2-((4-Methoxyphenyl)-diphenylmethylamino)ethyl]-N-[(N^4-(4-*tert*-butylbenzoyl)-cytosin-1-yl)acetyl] glycine (16). Compound **15** (1.63g; 2.28mmol) was dissolved in dioxane (10ml) and water (1ml). The solution was cooled to 0°C and 1M aqueous NaOH (4.56ml) was added dropwise in 2 aliquots. After 2h the solution was adjusted to pH5 by the dropwise addition of 2M aqueous $KHSO_4$. The precipitated salts were filtered off and washed with dioxane, and the combined filtrates were evaporated *in vacuo*. The residue was coevaporated twice with methanol and CH_2Cl_2. The residue was applied to a silica gel chromatography column and eluted with a gradient of 2-10% methanol and 1% triethylamine in CH_2Cl_2. **16** was obtained as an off-white foam in 0.83g (52%) yield. R_f =0.28 (CH_2Cl_2:MeOH/9:1). MS(FAB): 702.3282 ($C_{41}H_{43}N_5O_6$ + H requires 702.3292); ^1H NMR (d6-DMSO) δ 11.1 (1H, br s, cytosine H-4); 8.00 (3H, m, 2xtBuBz-H, cytosine H-6); 7.55 (2H, d, tBuBz H-3 and 5); 7.50-6.85 (15H, m, Mmt, cytosine H-5); 5.00 and 4.65 (2H, 2xs {rotamers}, N-CO-CH_2); 4.00 and 3.80 (2H, 2xs {rotamers}, N-CH_2- CO_2H); 3.70 (3H, s, Mmt-OMe); 3.45 (2H, m, CH_2-N); 2.15 (2H, m, MmtNH-CH_2); 1.30 (9H, s, tBu).

Methyl N-[2-((4-methoxyphenyl)-diphenylmethylamino)ethyl]-N-[(N^6-(4-methoxybenzoyl)-adenin-9-yl) acetyl] glycinate (17). Compound 3 (1.24g; 3.06mmol) was dissolved in DMF (7ml). To this solution was added NEM (1.06ml; 6.12mmol), HOOBt (0.498g; 3.06mmol), **9** (1.00g; 3.06mmol) and DIPC (0.58ml; 3.67mmol). The reaction mixture was stirred for 48h at 4°C. The solvent was evaporated *in vacuo*, and the residue was dissolved in ethyl acetate. This solution was washed twice with water and once with saturated aqueous KCl solution. The organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The resulting yellow foam was dissolved in a small volume of ethyl acetate and cooled on ice to induce crystallisation of N, N'-diisopropylurea, which was then removed by filtration. The residue was applied to a silica gel chromatography column which had been equilibrated with CH_2Cl_2:ethyl acetate/1:1, + 1% triethylamine, and eluted with CH_2Cl_2:ethyl acetate/1:1. **17** was obtained as a pale yellow-white foam in 1.75g (80%) yield. R_f =0.21 (CH_2Cl_2:MeOH/95:5). MS (FAB/MeOH/NBA/LiCl) 720.3 $[M+Li]^+$; ^1H NMR ($CDCl_3$) δ 8.95 (1H, br s, adenine

H-6); 8.75 and 8.70 (1H, 2xs {rotamers}, adenine H-2); 8.15 (1H, s, adenine H-8); 8.00 (2H, d, Anis H-2 and 6) 7.50-7.15 (12H, m, Mmt); 7.00 (2H, d, Anis H-3 and 5); 6.80 (2H, m, Mmt); 5.55 and 5.00 (2H, 2xs {rotamers}, N-CO-CH_2); 4.30 and 4.00 (2H, 2xs {rotamers}, N-CH_2- CO_2H); 3.90 (3H, s, Anis-OMe); 3.75 (3H, s, Mmt-OMe); 3.65 (5H, m, COOMe, CH_2-N); 2.35 (2H, m, MmtNH-CH_2).

N-[2-((4-Methoxyphenyl)-diphenylmethylamino)ethyl]-N-[(N^6-(4-methoxybenzoyl)-adenin-9-yl)acetyl] glycine (18). Compound **17** (1.70g; 2.38mmol) was dissolved in dioxane (10ml). The solution was cooled to 0°C and 1M aqueous NaOH (10.3ml) was added dropwise in 5 aliquots over 2.5h. After 2h at room temperature the solution was adjusted to pH5 by the dropwise addition of 2M aqueous $KHSO_4$. The precipitated salts were filtered off and washed with dioxane, and the combined filtrates were evaporated *in vacuo*. The residue was coevaporated twice with ethanol and CH_2Cl_2:methanol /9:1, (v/v). The residue was applied to a silica gel chromatography column and eluted with a gradient of 10-20% methanol and 1% triethylamine in CH_2Cl_2. **18** was obtained as a white foam in 1.62g yield (85%). R_f =0.10 (CH_2Cl_2:MeOH/8:2). MS(FAB): 700.2859 ($C_{39}H_{37}N_7O_6$ + H requires 700.2884); ^1H NMR ($CDCl_3$) δ 11.00 (1H, br s, adenine H-6); 8.70 and 8.65 (1H, 2xs {rotamers}, adenine H-2); 8.35 and 8.30 (1H, 2xs {rotamers}, adenine H-8); 8.05 (2H, dd, Anis H-2 and 6); 7.50-6.85 (16H, m, Mmt and Anis H-3 and 5); 5.55 and 5.15 (2H, 2xs {rotamers}, N-CO-CH_2); 4.05 and 3.90 (2H, 2xs {rotamers}, N-CH_2- CO_2H); 3.90 (3H, s, Anis-OMe); 3.75 (3H, s, Mmt-OMe); 3.40-3.65 (2H, m, COOMe, CH_2-N); 2.20 (2H, m, MmtNH-CH_2).

Methyl N-[2-((4-methoxyphenyl)-diphenylmethylamino)ethyl]-N-[(N^2-(isobutanoyl)-guanin-9-yl)-acetyl] glycinate (19). Compound **3** (1.45g; 3.59mmol) was dissolved in DMF (7ml). To this solution was added NEM (1.24ml; 7.17mmol), HOOBt (0.59g; 3.59mmol), **12** (1.00g; 3.59mmol) and DIPC (0.67ml; 4.31mmol). The reaction mixture was stirred for 48h at 4°C. The solvent was evaporated *in vacuo*, and the residue was dissolved in ethyl acetate. This solution was washed twice with water and once with saturated aqueous KCl solution. The organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The resulting yellow foam was dissolved in a small volume of ethyl acetate and cooled on ice to induce crystallisation of N, N'-diisopropylurea, which was then removed by filtration. The residue was applied to a silica gel chromatography column which had been equilibrated with CH_2Cl_2:ethyl acetate/1:1, + 1% triethylamine, and eluted with CH_2Cl_2:ethyl acetate/1:1. **19** was obtained as a pale yellow-white foam in 1.18g (49%) yield. R_f =0.13 (CH_2Cl_2:MeOH/95:5). MS (FAB/MeOH/NBA/LiCl) 678.3 $[M+2Li-H]^+$; 672.3 $[M+Li]^+$; ^1H NMR ($CDCl_3$) δ 11.80 (1H, br s, guanine H-2); 7.75 and 7.70 (1H, 2xs {rotamers}, guanine H-8); 7.55-6.80 (14H, m, Mmt); 5.45 and 4.90 (2H, 2xs {rotamers}, N-CO-CH_2); 4.25 and 4.00 (2H, 2xs {rotamers}, CH_2-CO_2Me); 3.75 (8H, m, Mmt-OMe, CO_2Me and CH_2-N); 2.30 (2H, m, MmtNH-CH_2); 1.90 (1H, septet, iBu-CH); 0.85 (6H, d, iBu-CH_3).

N-[2-((4-Methoxyphenyl)-diphenylmethylamino)ethyl]-N-[(N^6-(isobutanoyl)-guanin-9-yl)acetyl] glycine (20). Compound **19** (1.15g; 1.72mmol) was dissolved in dioxane (10ml). The solution was cooled to 0°C and 1M aqueous NaOH (10.3ml) was added dropwise in 5 aliquots over 2.5h. After 2h at room temperature the solution was adjusted to pH5 by the dropwise addition of 2M aqueous $KHSO_4$. The precipitated salts were filtered off and washed with dioxane, and the combined filtrates were evaporated *in vacuo*. The residue was coevaporated twice with ethanol and CH_2Cl_2:methanol/9:1, (v/v). The residue was applied to a silica gel chromatography column and eluted with a gradient of 10-20% methanol and 1% triethylamine in CH_2Cl_2. **20** was obtained as a white foam in 1.23g yield (95%). R_f =0.25 (CH_2Cl_2:MeOH/8:2). MS (-ES) 650.3 $[M-H]^-$. MS(FAB): 652.2883 ($C_{35}H_{37}N_7O_6$ + H requires 652.2884); ^1H NMR (d6-DMSO) δ 12.10 (1H, br s, guanine H-

2); 7.80 and 7.78 (1H, 2xs {rotamers}, guanine H-8); 7.45-6.85 (14H, m, Mmt); 5.20 and 4.95 (2H, 2xs {rotamers}, N-CO-CH_2); 3.95 and 3.80 (2H, 2xs {rotamers}, CH_2-CO_2H); 3.70 (3H, s, Mmt-OMe); 3.45 (2H, m, CH_2-N); 2.20 (3H, m, MmtNH-CH_2, iBu-CH); 0.85 (d, iBu-CH_3 and NEt_3).

1-Hydroxy-6-((4-methoxyphenyl)-diphenylmethylamino)-hexane (21). 6-Aminohexan-1-ol (1.00g; 8.55 mmol) was dissolved in anhydrous pyridine (7ml) and triethylamine(0.2ml). To this solution was added a solution of (4-methoxyphenyl)-diphenylmethyl chloride (2.50g; 8.12mmol) in anhydrous pyridine (9ml) in 3 aliquots at 45min intervals. The reaction was stirred at room temperature for a further 30min, then quenched by the addition of methanol (3ml). The solution was evaporated to a yellow syrup, and coevaporated 3 times with toluene to remove traces of pyridine. The residue was dissolved in ethyl acetate and washed with saturated aqueous $NaHCO_3$ solution, water and saturated aqueous KCl solution. The organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The residue was applied to a silica gel chromatography column and eluted with heptane:ethyl acetate:triethylamine/49.5:49.5:1, to give **21** in 1.64g (52%) yield. R_f =0.44 (heptane:ethyl acetate/1:1), 0.73 (CH_2Cl_2:ethyl acetate /1:1), 0.11 (CH_2Cl_2:MeOH/98:2). MS (FAB/NBA/LiCl) 396.3 $[M+Li]^+$, 390.3 $[M+H]^+$; ^1H NMR ($CDCl_3$) δ 7.50-6.80 (14H, m, Mmt); 3.80 (3H, s, OMe); 3.60 (2H, t, CH_2-O); 2.15 (2H, t, CH_2-N); 1.65-1.20 (8H, m, CH_2).

6-((4-Methoxyphenyl)-diphenylmethylamino)-hex-1-yl hemisuccinate (22). Compound **21** (1.00g; 2.57mmol) was dissolved in anhydrous pyridine (10ml). To this solution was added succinic anhydride (0.26g; 2.57mmol) and DMAP (31.3mg; 0.26mmol). After stirring for 3h at room temperature further succinic anhydride (25.7mg; 0.257mmol) and DMAP (62.6mg; 0.56mmol) were added and the solution was warmed to 50°C for 6h. After a further 16h at room temperature the solution was evaporated *in vacuo*. The residue was dissolved in ethyl acetate and washed once with an ice cold 5% aqueous solution of citric acid. The organic phase was dried (Na_2SO_4), filtered and evaporated *in vacuo*. The residue was applied to a silica gel chromatography column and eluted with 50% CH_2Cl_2/1% triethylamine in ethyl acetate, then with 5% methanol/1% triethylamine in CH_2Cl_2. **22** was obtained as a clear oil in 0.75g (60%) yield. R_f =0.30 (CH_2Cl_2:ethyl acetate/1:1). MS (-ES) 978.0 $[2M-H]^-$, 488.3 $[M-H]^-$. ^1H NMR ($CDCl_3$) δ 7.50-6.80 (14H, m, Mmt); 4.00 (2H, t, CH_2-O); 3.80 (3H, s, OMe); 2.60 (4H, m, CH_2-CH_2); 2.15 (2H, t, CH_2-N); 1.65-1.20 (8H, m, CH_2).

6-((4-Methoxyphenyl)-diphenylmethylamino)-hex-1-yl succinylamido-Tentagel. Amino-Tentagel™ (0.50g) was swollen for 10 min with a solution of NEM (0.10ml) and DMF (5ml), then filtered. A solution of **22** (97.4mg; 0.165mmol), NEM (15.9mg; 0.138mmol; 17.4µl) and TBTU (52.9mg; 0.165mmol) in DMF (3ml) was prepared and immediately added to the Tentagel™ NH_2. The resulting suspension was shaken for 16h at room temperature. The derivatised Tentagel was filtered off and washed with DMF (3x3ml), CH_2Cl_2 (3x1ml) and diethyl ether (3x1ml), then dried *in vacuo*. The Tentagel was capped by treatment with a solution of acetic anhydride, lutidine and 1-methyl imidazole in THF (1ml) for 1h. The derivatised and capped Tentagel was filtered off and washed with CH_2Cl_2 (3x1ml) and diethyl ether (3x1ml), then dried *in vacuo*. Qualitative Kaiser test showed the absence of free amines.

6-((4-Methoxyphenyl)-diphenylmethylamino)-hex-1-yl succinylamidopropyl-controlled-pore glass. Aminopropyl-CPG (550Å; 0.5g) was treated with a solution of NEM (0.1ml) and DMF (5ml) for 10min, then filtered. A solution of **22** (48.7mg; 0.082mmol), NEM (7.6µl) and TBTU (26.4mg; 0.082mmol) in DMF (3ml) was prepared and immediately added to the CPG. The resulting suspension was shaken for 16h at room temperature. The derivatised CPG was filtered off and washed with DMF (3x3ml), CH_2Cl_2 (3x1ml) and diethyl ether (3x1ml), then dried *in vacuo*. Capping and washing was carried out as for the Tentagel support.

Measurement of loading. The loading of the supports was determined by the spectrophotometric (478nm)determination of the concentration of Mmt^+ cations released by detritylation of a weighed sample of support. The literature[10] extinction coefficient of the Mmt cation: ε_{478} $(Mmt^+)=56 ml cm^{-1} \mu mol^{-1}$ was used for this calculation. The loading was calculated to be $168 \mu mol g^{-1}$ and $91 \mu mol g^{-1}$ for Tentagel and CPG, respectively.

Solid-phase synthesis of 12mer PNA sequence H_2N-aca tca tgg tcg-(hex). The monomers **14**, **16**, **18** and **20** were used for the synthesis of H_2N-aca tca tgg tcg-(hex) on a modified Eppendorf Biotronik Ecosyn™ D-300 DNA synthesizer on a 5µmol scale. The Mmt-protected hexyl succinylamidopropyl CPG described above was used as the solid support. The following synthesis conditions were used:

Deprotection of Mmt group: 3% Trichloroacetic acid in CH_2Cl_2 (3 min);

Neutralisation: 0.3M NEM in DMF;

Coupling of monomers: Monomer (0.3M solutions in DMF); NEM (0.3M solution in DMF); PyBOP as coupling reagent (0.3M solution in DMF), reagents pre-mixed in delivery syringe of synthesizer (15 sec); 30 min reaction time;

Capping: A:10% Acetic anhydride/10% lutidine in THF; B: 16% N-methyl imidazole in THF (the DNA capping reagents A and B are mixed just before use); capping time 1.5 min.

After synthesis was complete, the PNA was cleaved from the solid-support (2.5 hrs ambient temperature) and deprotected (6 hrs at 50°C) with conc. aqueous ammonia solution. Finally, cleavage of the Mmt group with 80% aqueous acetic acid gave the crude 12mer PNA sequence H_2N-aca tca tgg tcg-(hex). After concentration to dryness, the solid residue (electrospray mass spectrum of crude PNA m/z 3369.6; M(calculated for C_{135} H_{174} N_{70} O_{37}): 3369.31) was dissolved in 0.5ml 1M aqueous ammonia for HPLC purification. The PNA was almost insoluble in 0.5ml water. Purification on a LiChrospher™ WP300 RP-18(e) column (4x250mm; E. Merck, Darmstadt; Germany), eluting with a linear gradient of 10% to 35 % B in eluent A (A: 0.1% TFA in water; B: 0.1% TFA in 20% acetonitrile in water) resulted in 36% of homogeneous H_2N-acatcatggtcg-(hex). Positive ion electrospray mass spectrum m/z 3369.16±0.33; M(calculated for C_{135} H_{174} N_{70} O_{37}): 3369.31.

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Synthesis of α-(Alkoxysilyl)acetic Esters. A Route to 1,2 Diols.

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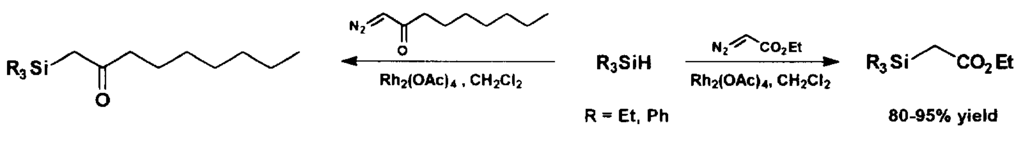
Abstract : An easy route to α-(alkoxysilyl)acetic esters and their utilization is described. It involves a two-step sequence carried out in one pot : Rhodium catalyzed Si-H insertion of a carbenoid, generated by decomposition of N_2CHCO_2Et, followed by a nucleophilic attack onto the Si-Cl bond by an alcohol. Alkylation of the title esters, reduction of the ester function and finally oxidation of the C-Si bond provide a facile entry to 1,2-diols.

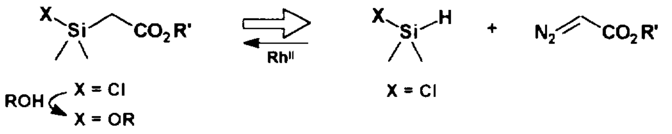
α-Silyl carbonyl compounds have been mostly used as enolate equivalents[1] or as precursors of α,β-unsaturated esters and substituted ketones, generated through the Peterson elimination.[2,3] The loss of the silicon moiety in these transformations is greatly facilitated by the presence of the vicinal electron-withdrawing carbonyl group. The discovery that the silicon group could be oxidized into a hydroxyl group[4] and not just eliminated or replaced by a proton, led to a renewed interest in this class of compounds.[5]

α-Silyl carbonyl compounds are accessible using different approaches, such as oxidation of β-hydroxysilanes,[6] condensation of α-silyl organometallic reagents with carbonyl compounds,[7] rearrangements[8] and C-silylation of esters, carboxylic acids, amide enolates,[9] and hydrazones.[5a,b] This last method is efficient for the preparation of α-silylamides and α-silylhydrazones but is rather limited for the preparation of α-silyl esters due to the large amount of *O*-silylation generally observed in this case. Decomposition of α-diazo carbonyl derivatives in the presence of organosilanes catalyzed by transition metal such as copper (Cu powder ou CuCl) has also been reported but generally gives low yields of the corresponding α-silylacetic esters.[10] In 1988, Doyle and co-workers reexamined this reaction and found that $Rh_2(OAc)_4$ catalyzed decomposition of α-diazocarbonyl compounds led to excellent yields of α-silylesters and α-silyl-ketones through insertion of a rhodium-carbenoid species into the Si-H bond (Scheme 1).[11]



Scheme 1

From the perspective of using the silicon group on the ester fragment as a masked hydroxyl group, we thought that it might be useful to devise an approach to α-silylacetic esters possessing better nucleofugal groups on silicon, than Ph or Et groups used by Doyle et al. Tamao and co-workers effectively demonstrated that the oxidation conditions required for the conversion of a Si-OR group into a OH group are generally very mild and thus leave most functionalities untouched.[4a,b] Our first attempts to prepare α-(alkoxysilyl)acetic esters directly from $(EtO)_3SiH$ and N_2CHCO_2Et catalyzed by $Rh_2(OAc)_4$, failed to afford the desired compounds. Repeating the reaction with $(i\text{-PrO})Me_2SiH$ gave only 30% of the α-(isopropyloxydimethylsilyl)acetic ester along with dimerization products from the diazoester. As alkoxy groups might interfere with transition metal catalysis or decrease the reactivity of the Si-H bond, we turned our attention to the readily available chlorosilanes. Chlorine should not alter the catalyst activity by coordination and can be easily displaced by alkoxy groups after the insertion process to form the desired α-(alkoxysilyl)acetic ester compounds (Scheme 2).



Scheme 2

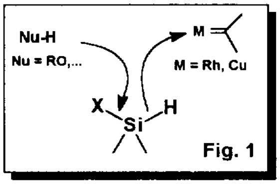
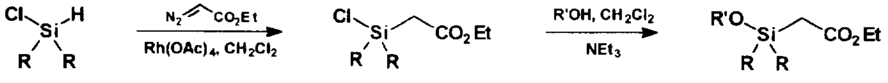


Fig. 1

In a preliminary account, we demonstrated that the dual reactivity of chlorosilanes (Fig. 1) affords an efficient approach to the title compounds.[12a] We report herein a full description of our studies directed towards the synthesis of α-(alkoxysilyl)acetic esters and their use as precursors of 1,2-diols.

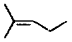
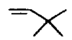
The synthesis of α-(alkoxysilyl)acetic esters was carried out in one pot (Scheme 3), by slowly adding (using a syringe pump) the α-diazoester to a mixture of chlorosilane and a catalytic amount of $Rh_2(OAc)_4$ in anhydrous CH_2Cl_2. A faster addition usually induced the dimerization of the carbenoid species and the formation of diethyl fumarate and maleate. The chlorosilane intermediate, which can be isolated in quantitative yield in most cases, was then treated with the appropriate alcohol R'OH and a base (e.g. NEt_3) in dry CH_2Cl_2. The workup and distillation gave the desired alkoxysilane in good yields as summarized in Table 1.



1

Scheme 3

Table 1. Preparation of α-(alkoxysilyl)acetic esters 1 (Scheme 3).

Entry	Chlorosilane (R)	Alcohol (R')	Conditions[a]	Product	Yield[b]
1	Me	i-Pr	A	**1a**	74
2	Me	Bn	A	**1b**	76
3	Me	Et	A	**1c**	73
4	Me	t-Bu	A	**1d**	78
5	Me	allyl	A	**1e**	71
6	Ph	Et	A	**1f**	74
7	Ph	i-Pr	A	**1g**	65
8	Me		A	**1h**	80
9	Me		A	**1i**	82
10	Me	 Ph	A	**1j**	75
11	i-Pr	Et	B	**1k**	70
12	t-Bu	Et	B	**1l**	62[c]

[a] Conditions A: R_2SiClH (1.05 eq.), $Rh_2(OAc)_4$ (0.3 mol%), N_2CHCO_2Et (1 eq.) then NEt_3 (1.2 eq.) and R'OH (1.2 eq.) in anhydrous CH_2Cl_2.

Conditions B: Insertion carried out as in Conditions A. The chlorosilane was then added to a mixture of EtOH (5 eq.), imidazole (3 eq.) and 4-DMAP (cat.) in dry DMF.

[b] Isolated yields after filtration through Florisil® or distillation. [c] Accompanied together with 20% of the corresponding silanol : ethyl-2-(di-*t*-Butylhydroxysilyl)ethanoate (see Experimental section).