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Structural characterisation of trimethylsilyl-protected DNA bases

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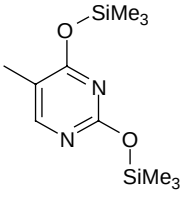
The structures of the silylated DNA bases, bis(trimethylsilyl)thymine (**1**), bis(trimethylsilyl)cytosine (**2**), bis(trimethylsilyl)adenine (**3**) and tris(trimethylsilyl)guanine (**4**), have been determined. **1** is *O*-silylated and displays no intermolecular interactions. **2** is silylated at both exocylic *O*, *N* positions and forms a chain structure through intermolecular NH···O and NH···N hydrogen bonds. **3** contains two $SiMe_3$ groups, on the exocylic NH and endocyclic N^9 position, respectively; of two independent molecules in the asymmetric unit, one dimerises through complementary NH···N hydrogen bonds, while the other forms a strained intramolecular hydrogen bond through the same pair of donor and acceptor centres. **4** incorporates *N*, *N*, *O*–$SiMe_3$ moieties and forms chains via bifurcated CH···O/N hydrogen bonds, while the NH function remains unexploited. The effects of silylation on these pyrimidine and purine ring structures are also discussed in comparison with the native bases.

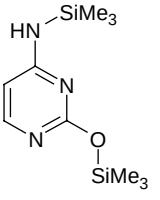
Keywords: silylated DNA bases, thymine; cytosine; guanine; adenine; X-ray structure determinations

Introduction

DNA bases are difficult compounds to work with because of their limited solubility in common organic solvents. The formation of trimethylsilyl-substituted bases (**1**–**4**) alleviates this problem and thus provide a synthetic entry point for further DNA base elaboration. However, despite their synthetic utility, these silylated bases have never been structurally characterised. In addition, the partial blocking of various hydrogen bonding sites should give rise to novel supramolecular architectures. Moreover, despite their biological importance, structural data on the four key pristine DNA bases are relatively scarce, since in many instances data for ionic derivatives have been reported, presumably because of the solubility enhancement such species enjoy. In addition to these ionic derivatives, structural data have been reported for thymine (*1*) and cytosine (*2*), while those data for adenine and guanine relate to their monohydrates (*3*, *4*). Thus, it was of interest to synthesise crystalline samples for X-ray diffraction, in order to both further investigate the hydrogen bonding modes of these substituted DNA bases and expand the range of structural data available for the neutral bases in general.



(**1**)



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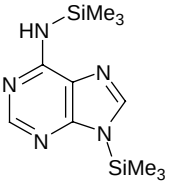
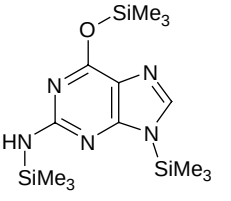


(**3**)



(**4**)

Results and discussion

The synthesis of **1**–**4** followed a previously reported route, refluxing a stoichiometric excess of hexamethyldisilazane (HMDS) with the DNA base in the presence of catalytic amounts of ammonium sulphate (*5*). The melting points of **1** and **2** compared well with the literature values (*5*, *6*), but that of **3** was significantly higher than those reported previously (*6*). The ^1H and $^{13}C\{^1H\}$ NMR spectra of the four compounds were unremarkable, showing singlets due to Me_3Si near $\delta = 0$ ppm and resonances due to the base in good correlation with the literature (*7*). Of greater interest, however, were the ^{29}Si NMR spectra of the compounds, which illustrate well the different environments in which

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silicon is found in the protected compounds. The preference for Si—O bond formation, driven by the relative strengths of Si—O and Si—N bonds (466 (*8*) and 439 kJ mol^{-1} (*9*), respectively), is apparent in these spectra and confirmed by the crystallography. Me_3Si—O linkages are typified by δ(^{29}Si) at *ca.* 20 ppm (**1**: 20.8, 22.8; **2**: 20.9; **4**: 23.6 ppm), while Me_3Si—NH and Me_3Si—N environments give rise to resonances at *ca.* 5 and 14 ppm, respectively (**2**: 7.2; **3**: 7.2, 14.3; **4**: 3.4, 13.4 ppm). The case of guanine (**4**), which incorporates all three distinct Me_3Si environments, is exemplary in this respect. The data correlate well with the literature values (*10*), and are consistent with δ(^{29}Si) in model compounds [Me_3SiOPh: 19.2 (*11*), $(Me_3Si)_2NH$: 2.1 (*12*), $Me_3SiN_{pyrrole}$: 12.0 ppm (*7*)).

Structure of bis(trimethylsilyl)thymine (1)

The molecular structure of **1** is illustrated in Figure 1; selected bond lengths and angles are presented in Table 1. The structure of the molecule is monomeric, with no intermolecular interactions. The two $SiMe_3$ groups have protected the carbonyl groups, the silicon atoms lying in the plane of the molecule, with relatively long bond distances [Si(1)–O(1): 1.6906(16), Si(2)–O(2): 1.6951(16) Å] compared with silyl ether bonds in similar compounds (*13–15*) such as in *hexa*-(trimethylsiloxy)benzene [Si–O 1.655(3): 1.673(4) Å] (*15*). The bulk of the $SiMe_3$ group has forced it away from the ring, enlarging the C–O–Si bond angle [C(1)–O(1)–Si(1): 125.40(14)°, C(5)–O(2)–Si(2): 125.46(14)°] from the expected tetrahedral value.

There are significant changes in the structure of the pyrimidine ring on silylation, which result in complete conjugation of π-bonds around the heterocycle. The C═O double bonds [C(1)–O(1): 1.244(4), C(5)–O(2): 1.225(4) Å] (*1*) both become C–OSi single bonds on substitution, and there is an evident bond lengthening as a result [1.341(3), 1.337(3) Å, respectively]. Within the heterocycle, all the bonds shorten on substitution (Table 1) as a result of developing π-bond character, save for C(2)–C(3), whose bond order is reduced from 2 by involvement in the delocalisation of the double bond character around the ring and as a result becomes longer than that in thymine [1.371(3) vs. 1.343(4) Å] (*1*). There is also a major rearrangement of bond angles upon silylation. While the bond angles at C(2) and C(3), which are largely unaffected by the aromatisation of the ring, are only slightly perturbed, those angles at N(1), C(1), N(2) and C(5) alter dramatically. In thymine, the four ring angles divide into two groups: narrow angles at the carbonyl carbons of *ca.* 115° and wider angles at the NH functions of *ca.* 124°. Upon silylation, this trend reverses, with an opening of the ring angles at the carbonyl groups [N(1)–C(1)–N(2): 127.29(19), C(3)–C(5)–N(2): 123.5(2)°], while the angles at the deprotonated nitrogens diminish to *ca.* 115° [C(1)–N(2)–C(2): 114.85(19), C(1)–N(2)–C(5): 115.63(18)°]. These changes can be readily understood on simple valence shell electron pair repulsion (VSEPR) grounds. In thymine, the C═O concentrates electron density around carbon closing the bond angle at the latter, while the N—H bond pair is stereochemically less influential. In contrast, in **1**, the exocyclic C—OSi bond pair does not compress the angle at carbon the way the C═O does allowing it to open,

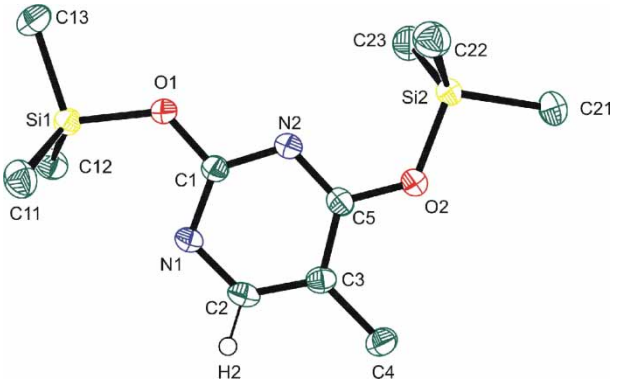

Figure 1. The asymmetric unit of **1**; ellipsoids are at the 50% probability level. Hydrogen atoms of the Me_3Si groups omitted for clarity.

Table 1. Selected bond lengths (Å) and angles (°) for bis(trimethylsilyl)thymine (**1**).

		Thymine[a]
Lengths		
C(1)–O(1)	1.341(3)	1.244(4)
O(1)–Si(1)	1.6906(16)	
C(5)–O(2)	1.337(3)	1.225(4)
O(2)–Si(2)	1.6951(16)	
C(1)–N(1)	1.327(3)	1.358(4)
C(1)–N(2)	1.338(3)	1.361(4)
C(2)–N(1)	1.353(3)	1.384(5)
C(2)–C(3)	1.371(3)	1.343(4)
C(3)–C(5)	1.406(3)	1.453(4)
C(3)–C(4)	1.501(2)	1.502(4)
C(5)–N(2)	1.327(3)	1.401(5)
Angles		
C(1)–O(1)–Si(1)	125.40(14)	
C(1)–N(1)–C(2)	114.85(19)	122.5(3)
C(1)–N(2)–C(5)	115.63(18)	126.3(3)
N(1)–C(1)–O(1)	118.24(18)	122.4(3)
N(1)–C(1)–N(2)	127.29(19)	115.5(2)
N(2)–C(1)–O(1)	114.47(19)	122.0(3)
C(5)–O(2)–Si(2)	125.46(14)	
C(5)–C(3)–C(2)	114.5(2)	118.4(3)
N(2)–C(5)–O(2)	118.28(19)	119.2(3)
N(2)–C(5)–C(3)	123.5(2)	115.1(3)
C(3)–C(5)–O(2)	118.3(2)	125.7(3)
N(1)–C(2)–C(3)	124.1(2)	122.3(3)
C(4)–C(3)–C(5)	121.9(2)	118.3(3)
C(2)–C(3)–C(4)	123.6(2)	123.3(3)

[a] Ref. (*1*).

while the lone pair which results at N(1), N(2) upon silylation at oxygen causes the interior bond angle at these nitrogens to compress.

Structure of bis(trimethylsilyl)cytosine (2)

The molecular structure of **2** is illustrated in Figure 2; selected bond lengths and angles are presented in Table 2. The asymmetric unit of the crystal consists of two molecules of **2**, held together by an N—H···N hydrogen bond. The $SiMe_3$ groups have protected the carbonyl and primary amine groups, with the Si atoms in the plane of the six-membered ring, as in **1**. The Si–N bonds [Si(1)–N(1): 1.748(2), Si(4)–N(4): 1.742(2) Å] compare well with the length of Si—N in known compounds such as *N*-(2-phenoxyphenyl)-*N*-(trimethylsilyl)amine [Si—N 1.745(1) Å] (*16*), but the Si—O bond lengths [Si(2)—O(1): 1.667(2), Si(3)–O(2): 1.6775(19) Å] are slightly longer than the known comparators (*13–15*), e.g. in *hexa*-(trimethylsiloxy)benzene [Si—O: 1.655(3) Å] (*15*). The Si—O bond distance is slightly shorter than those found in **1** [1.6906(16), 1.6951(16) Å], suggesting a stronger interaction between the $SiMe_3$

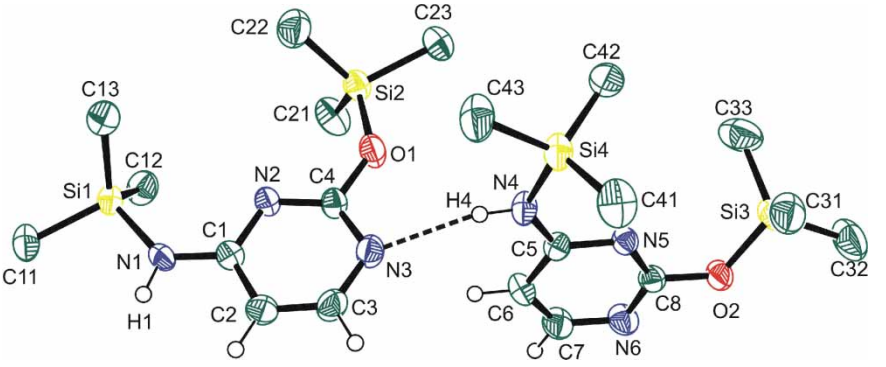

Figure 2. The asymmetric unit of **2**; ellipsoids are at the 50% probability level. Hydrogen atoms of the Me_3Si groups omitted for clarity.

Table 2. Selected bond lengths (Å) and angles (°) for bis(trimethylsilyl)cytosine (**2**).

				Cytosine[a]
Lengths				
Molecule 1		Molecule 2		
Si(1)–N(1)	1.748(2)	Si(4)–N(4)	1.744(2)	
Si(2)–O(1)	1.667(2)	Si(3)–O(2)	1.6773(19)	
C(1)–N(1)	1.358(4)	C(5)–N(4)	1.353(3)	1.330(3)
C(1)–N(2)	1.350(3)	C(5)–N(5)	1.354(3)	1.337(3)
C(1)–C(2)	1.402(4)	C(5)–C(6)	1.399(4)	1.424(3)
C(2)–C(3)	1.358(4)	C(6)–C(7)	1.356(4)	1.342(3)
C(3)–N(3)	1.341(4)	C(7)–N(6)	1.347(4)	1.357(3)
N(3)–C(4)	1.322(3)	N(6)–C(8)	1.322(3)	1.374(3)
C(4)–N(2)	1.338(3)	C(8)–N(5)	1.330(3)	1.364(3)
C(4)–O(1)	1.349(3)	C(8)–O(2)	1.362(3)	1.234(3)
Angles				
Molecule 1		Molecule 2		
C(1)–N(1)–Si(1)	131.7(2)	C(5)–N(4)–Si(4)	129.94(19)	
C(4)–O(1)–Si(2)	133.38(17)	C(8)–O(2)–Si(3)	128.38(17)	
N(1)–C(1)–N(2)	119.0(2)	N(4)–C(5)–N(5)	118.1(2)	118.2(2)
N(1)–C(1)–C(2)	120.5(2)	N(4)–C(5)–C(6)	121.4(2)	119.9(2)
C(2)–C(1)–N(2)	120.4(3)	C(6)–C(5)–N(5)	120.4(3)	122.0(2)
C(1)–C(2)–C(3)	117.4(3)	C(5)–C(6)–C(7)	117.3(3)	117.3(2)
C(2)–C(3)–N(3)	123.7(3)	C(6)–C(7)–N(6)	124.1(3)	120.1(2)
C(3)–N(3)–C(4)	114.2(2)	C(7)–N(6)–C(8)	113.5(3)	122.7(2)
N(2)–C(4)–O(1)	118.3(2)	N(5)–C(8)–O(2)	116.9(2)	122.2(2)
N(3)–C(4)–O(1)	113.0(2)	N(6)–C(8)–O(2)	113.9(2)	119.8(2)
N(2)–C(4)–N(3)	128.7(3)	N(5)–C(8)–N(6)	129.2(3)	118.1(2)
C(1)–N(2)–C(4)	115.5(2)	C(5)–N(5)–C(8)	115.5(2)	119.9(2)

[a] Ref. (*2*).

group and the lone oxygen of cytosine than with the two available sites on thymine. The bulk of the $SiMe_3$ groups has caused the C—O—Si and C—N—Si bond angles to widen from the tetrahedral [C(4)–O(1)–Si(2): 133.40(17), C(1)–N(1)–Si(1): 131.6(2)°] and accommodate them, though to a greater degree than in **1** in both cases. In the case of the C—O—Si bond angle, this may well be due to the relative shortness of the Si—O bond compared with **1** creating greater steric hindrance between the protecting group and the ring, and causing the bond angle to widen to provide greater relief. In addition, the exocyclic C—N(H)$SiMe_3$ bond [C(1)–N(1): 1.359(4) Å] has lengthened slightly with respect to the C—NH_2 in cytosine [1.330(3) Å] (*2*), again reflecting the molecular congestion caused by silylation, while the elongation of the C—O bond on silylation (change from C═O to C—O) is also evident as it was with thymine.

As with thymine, silylation of cytosine induces aromatisation of the pyrimidine ring with the same trends in effects (Table 2). There is a shortening of all the bonds within the ring with the exception of C(2)–C(3) which lengthens; the bond angles at C(4, 8) open [128.7(3), 129.(3) vs. 118.1(2)° in cytosine], while those at N(3, 6) close [114.2(3), 113.5(3) vs. 122.7(2)°] all for the reasons outlined above with respect to thymine. In contrast to thymine but consistent with these arguments, the internal angles at C(1) and C(5) remain largely unaltered from those in cytosine (Table 2), as C—NH_2 is converted to C—N(H)$SiMe_3$ (both have exocyclic single bonds) which contrasts with the C═O to C—$OSiMe_3$ change in thymine (double to single bond).

The molecule forms a helical polymeric chain (Figure 3(a); Table 3) with a pitch of 21.7 Å (compared with 34 Å in β-DNA) (*17*), interacting via alternating straight NH···O [2.26(3) Å] and NH···N [2.24(3) Å] hydrogen bonds [N(1)–H(1)···O(2) 173.9(1), N(4)–H(4)···N(3) 168.1(1)°], of slightly longer length to hydrogen bonds in other cytosine compounds (*18–21*) such as 1-methylcytosine [H—O 2.04(2), H—N 2.14(2) Å] (*18*). The pitch involves a four molecule turn (Figure 3(b)).

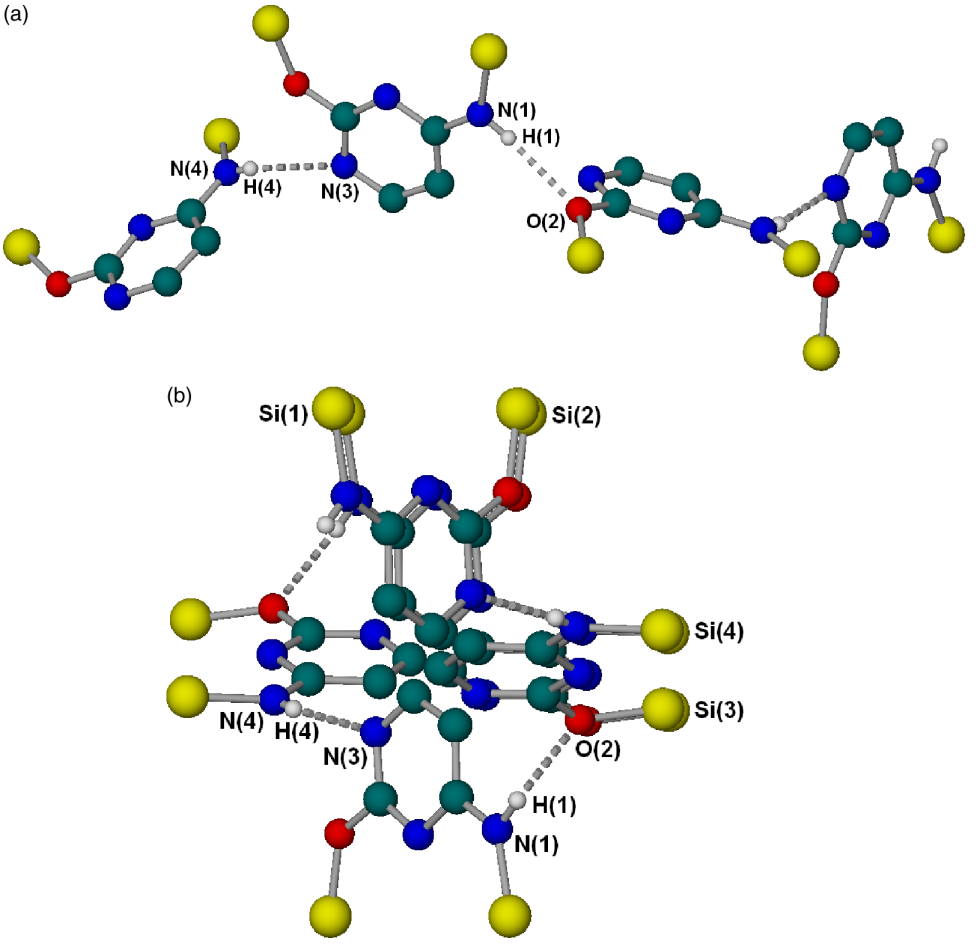

Figure 3. The helical chain structure of **2** viewed (a) orthogonal to and (b) along the axis of propagation. Symmetry operator (3/2) − *x*, 1 − *y*, (1/2) + *z*.

Table 3. Hydrogen bonding interactions.

	D—H	d(D—H)	A	d(H···A)	d(D···A)	<D—H···A	Symmetry operation
(**2**)	N(1)–H(1)	0.80(3)	O(2)	2.33(3)	3.133(3)	175(3)	$-x+1, y-(1/2), -z+(1/2)$
	N(4)–H(4)	0.865(10)	N(3)	2.253(12)	3.102(3)	167(3)	$x-(1/2), -y+(3/2), -z$
(**3**)	N(1)–H(1)	0.81(3)	N(4)	2.38(3)	3.172(3)	169(2)	$-x, y, (1/2)-z$
	N(6)–H(6)	1.003(19)	N(9)	2.53(2)	3.066(3)	113.3(14)	
(**4**)	C(3)–H(3)	1.04(7)	N(1)	2.38(7)	3.257(8)	142(5)	$(3/2)-x, -(1/2)+y, (1/2)-z$
	C(3)–H(3)	1.04(7)	O	2.63(7)	3.463(7)	137(5)	$(3/2)-x, -(1/2)+y, (1/2)-z$

Structure of bis(trimethylsilyl)adenine (3)

The molecular structure of **3** is illustrated in Figure 4; selected bond lengths and angles are presented in Table 4. The asymmetric unit consists of two independent molecules. In both the cases, the two $SiMe_3$ groups have protected the primary [N(1)–Si(1) 1.751(2) Å] and secondary [N(5)–Si(2) 1.794(2) Å] exocyclic amine groups, with the Si atoms in the plane of the purine ring. The Si—N bond length in the protected primary amine compares well with that of **2** [1.749(3) Å] and other similar Si—N bonds such as in *N*-(2-phenoxyphenyl)-*N*-(trimethylsilyl)amine [Si—N 1.745(1) Å] (*16*). The Si—N length in the protected secondary amine is, however, long compared with that of known compounds which could serve as analogues, such as chloro-3-(*N*-(tri-isopropylsilyl)pyrrole)-mercury [Si—N 1.775(2) Å] (*22*).

The steric bulk of the $SiMe_3$ group protecting the primary amine causes the C—NH—Si moiety to deform slightly to accommodate a wide C—N—Si bond [C(1)–N(1)–Si(1) 127.26(19)°] compared with the corresponding C—N—H bond in 9-methyladenine [C(1)–N(1)–H(1) 120.2(1)°] (*23*). In general, however, comparison of the metrical data for **3** with those of adenine monohydrate (*3*) shows only minor variations, perhaps not unexpectedly since the distribution of electron density around the purine is not compromised by bis-silylation at the two nitrogens, unlike the cases for thymine and cytosine where *O*-silylation induces π-delocalisation around the pyrimidine. One point of similarity between **3** and the cytosine derivative (**2**) is an elongation of the exocyclic C—N(H)$SiMe_3$ bond [C(1)–N(1): 1.363(3), C(6)–N(6): 1.368(3) Å] compared with adenine [1.339(3) Å] (*3*).

The two molecules in the asymmetric unit, rather surprisingly, behave differently with regard to their supramolecular chemistry. The molecule based on Si(1, 2) forms a dimer held together by two symmetry-related N—H···N hydrogen bonds [N(1)–H(1)···N(4): 2.38(1), N(1)–H(1)···N(4) 169(2)°] (Figure 5(a)). These are longer than the NH···N hydrogen bonds founds in 2-methylcytosine (2.26(3), 2.24(3) Å) and 1-methylcytosine (2.14(2) Å) (*18*). The bulk of the $SiMe_3$ groups protecting the amines is also the driving force behind the orientation of the molecules within the dimer. The planes of the two adenine molecules lie approximately

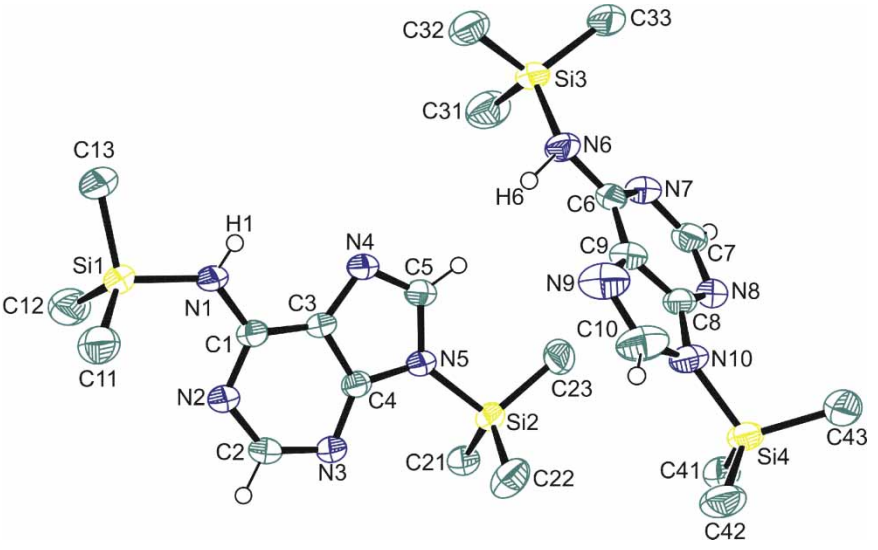

Figure 4. The asymmetric unit of **3** showing the two independent molecules in the asymmetric unit; ellipsoids are at the 50% probability level. Hydrogen atoms of the Me_3Si groups omitted for clarity. Symmetry operator $1-x, y, (1/2)-z$.

Table 4. Selected bond lengths (Å) and angles (°) for bis(trimethylsilyl)adenine (**3**).

				Adenine·H_2O[a,b]
Lengths				
Molecule 1		Molecule 2		
Si(1)–N(1)	1.751(2)	Si(3)–N(6)	1.760(2)	
Si(2)–N(5)	1.794(2)	Si(4)–N(10)	1.784(2)	
C(1)–N(1)	1.363(3)	C(6)–N(6)	1.368(3)	1.339
C(1)–N(2)	1.347(3)	C(6)–N(7)	1.344(3)	1.359
C(1)–C(3)	1.392(4)	C(6)–C(9)	1.405(4)	1.415
N(2)–C(2)	1.337(3)	N(7)–C(7)	1.333(3)	1.344
C(2)–N(3)	1.326(3)	C(7)–N(8)	1.330(3)	1.331
N(3)–C(4)	1.344(3)	N(8)–C(8)	1.332(4)	1.349
C(3)–C(4)	1.383(3)	C(9)–C(8)	1.383(4)	1.394
C(4)–N(5)	1.384(3)	C(8)–N(10)	1.389(3)	1.368
C(5)–N(5)	1.380(3)	C(10)–N(10)	1.338(4)	1.358
C(3)–N(4)	1.391(3)	C(9)–N(9)	1.387(4)	1.394
C(5)–N(4)	1.309(3)	C(10)–N(9)	1.331(4)	1.325
Angles				
Molecule 1		Molecule 2		
C(1)–N(1)–Si(1)	127.26(19)	C(6)–N(6)–Si(3)	127.1(2)	
N(1)–C(1)–N(2)	118.7(2)	N(6)–C(6)–N(7)	120.2(2)	118.3
N(1)–C(1)–C(3)	123.1(2)	N(6)–C(6)–C(9)	120.5(3)	124.3
N(2)–C(1)–C(3)	118.2(2)	N(7)–C(6)–C(9)	119.3(2)	117.4
C(1)–N(2)–C(2)	117.4(2)	C(6)–N(7)–C(7)	116.5(2)	118.7
N(2)–C(2)–N(3)	130.3(2)	N(7)–C(7)–N(8)	130.3(3)	129.3
C(2)–N(3)–C(4)	110.3(2)	C(7)–N(8)–C(8)	111.5(2)	111.2
N(3)–C(4)–N(5)	126.9(2)	N(8)–C(8)–N(10)	126.5(2)	128.0
N(3)–C(4)–C(3)	126.1(2)	N(8)–C(8)–C(9)	125.6(2)	126.2
C(1)–C(3)–C(4)	117.5(2)	C(6)–C(9)–C(8)	116.9(2)	117.2
C(1)–C(3)–N(4)	132.0(2)	C(6)–C(9)–N(9)	133.8(3)	132.3
C(4)–C(3)–N(4)	110.4(2)	C(8)–C(9)–N(9)	109.3(2)	110.5
C(4)–N(5)–C(5)	103.81(19)	C(8)–N(10)–C(10)	103.6(2)	106.4
C(4)–N(5)–Si(2)	127.05(16)	C(8)–N(10)–Si(4)	128.1(2)	
C(5)–N(5)–Si(2)	128.81(18)	C(10)–N(10)–Si(4)	128.3(2)	
N(4)–C(5)–N(5)	115.4(2)	N(9)–C(10)–N(10)	116.3(3)	114.2
C(5)–N(4)–C(3)	103.3(2)	C(10)–N(9)–C(9)	103.0(3)	103.2

[a] Ref. (*3*).
[b] Estimated average esds: 0.003 Å, 0.2°.

perpendicular to each other (Figure 5(b)), orientating the $SiMe_3$ groups as far from each other as possible. In contrast, the molecule based on Si(3, 4) forms no intermolecular hydrogen bonds, but there is a strained intramolecular contact between H(6) and N(9) (Figure 4, Table 3).

Structure of tris(trimethylsilyl)guanine (4)

The molecular structure of **4** is illustrated in Figure 6; selected bond lengths and angles are presented in Table 5. The three $SiMe_3$ groups have protected the primary [N(4)–Si(3): 1.740(4) Å] and secondary [N(2)–Si(2): 1.778(4) Å] amine groups, and the carbonyl group [O–Si(1): 1.665(4) Å], with the Si atoms in the plane of the purine rings, as in **3**. The Si—O distance compares well with the Si–O bond distances in similar silyl ethers (*13–15*) such as *hexa*-(trimethylsiloxy)benzene [Si—O 1.655(3) Å] (*15*) and **2** [1.667(2) Å], though shorter than the Si—O distances in **1** [1.6906(16), 1.6951(16) Å]. The Si—N distance in the primary amine compares well with **2** [1.749(3) Å], **3** [1.750(2) Å] and known compounds such as *N*-(2-phenoxyphenyl)-*N*-(trimethylsilyl)amine [Si—N 1.745(1) Å] (*16*). The Si—N distance in the secondary amine is similar to that in related species, such as chloro-3-(*N*-(tri-isopropylsilyl)pyrrole)-mercury [1.775(2) Å] (*22*).

Upon silylation, the exocyclic C(1)–O(1) bond is reduced in order and correspondingly lengthens with respect to guanine, as also seen in **1** and **2** (Table 5). Similarly, the C(5)–N(4) bond to the exocyclic primary amine also lengths significantly upon silylation (Table 5), again a feature present in the structures of **2** and **3**, but more markedly so in the case of **4** [C(5)–N(4): 1.380(6) vs. 1.358(4), average 1.367(3) Å, for **2** and **3**, respectively]. The effects of silylation on the bond lengths and angles with the purine rings are entirely consistent with what might be expected in the light of

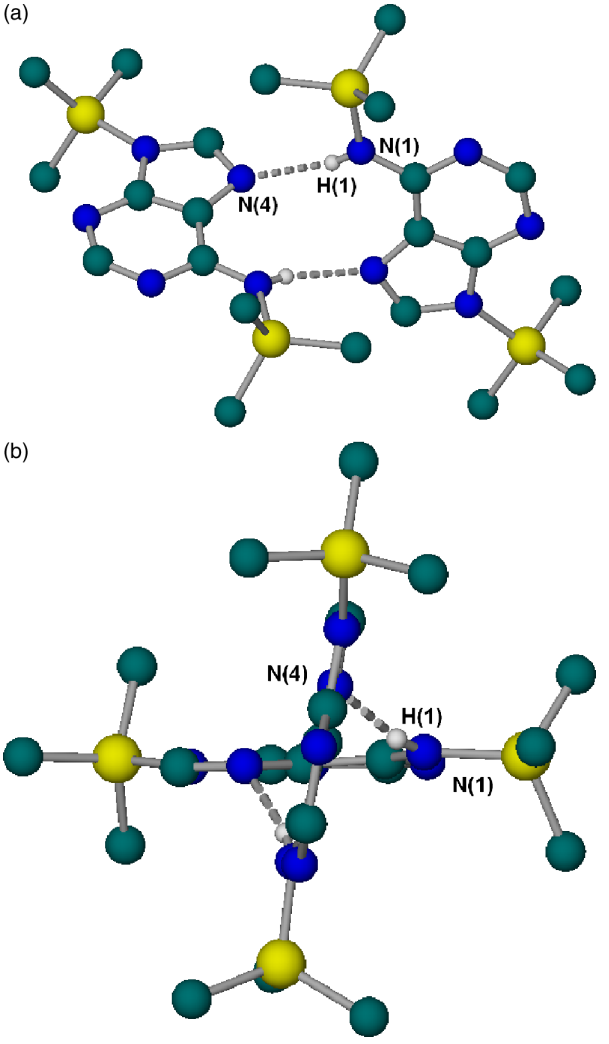

Figure 5. Two views of the dimerisation of one of the independent molecules of the asymmetric unit of **3**.

structures **1**–**3**. Those bonds that change from nominal single bonds in guanine to part of a delocalised π-system in **4** all shorten [C(1)–N(5), C(1)–C(2), C(2)–N(1),C(4)–N(2), C(5)–N(5)], but there are no significant changes to those bonds that already incorporate double bond character in the parent base [N(3)–C(5), C(2)–C(4)] (Table 5). However, a note of caution should be added to these comments, as the high estimated standard deviations (esds) associated with these bond lengths make anything other than a general observation unreasonable. Similarly, with the changes in bond angles, the trends mimic those already noted in the structures of **1** and **2**: the angle at C(1)–O(1) expands from 111.9(2)° in guanine monohydrate to 120.4(4)° in **4** as the C═O is reduced in bond order, while the C—N—C angle at the endocyclic secondary amine N(5) contracts from 124.6(2)° in the parent to 117.2(4)° in **4** as the exocyclic N—H bond pair is replaced by a spatially more demanding lone electron pair.

The supramolecular structure of **4** involves a polymer held together by bifurcated C—H···N and C—H···O hydrogen bonds C(3)–H(3)···N(1): 2.38(7) Å; C(3)–H(3)···N(1): 142(5)°; C(3)–H(3)···O: 2.63(7) Å; C(3)–H(3)···O: 137(5)°], forming a zigzag chain (Figure 7). This orientation is probably adopted on steric grounds to keep the $SiMe_3$ groups as far from each other as possible, as in **3**. The formation of hydrogen bonds between nitrogen/oxygen and a relatively unpolarised hydrogen attached to carbon is surprising, due to the presence of an available N—H on the protected exocylic amine N(4) (which, remarkably, does not involve itself in H bonding), but not unknown. The preference for these weaker hydrogen bonding interactions appears to be to locate the bulky Me_3Si groups on the exterior of the propagating chain (Figure 7(b)), in a similar fashion to polymeric silylated cytosine (**2**) and dimeric silylated adenine (**3**).

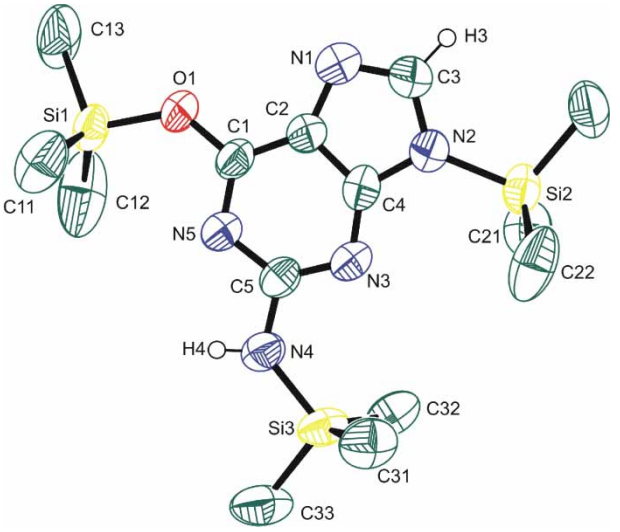

Figure 6. The asymmetric unit of **4**; ellipsoids are at the 50% probability level. Hydrogen atoms of the Me_3Si groups omitted for clarity.

Comparison of the C—H···N hydrogen bond in **4** with a range of known examples of C—H···N bonds [C—H···N: 2.44–2.98] (*24*) suggests that they are strong for this type of interaction, and compare well with some of the shorter interactions of this type such as those in methylpyrazine [C—H···N: 2.44(2)–2.76(2) Å] (*24*). The sum of the van der Waals radii of H and N is 2.75 Å (*25*). The history of C—H···O hydrogen bonds and their use in crystal engineering have been recently reviewed (*26*, *27*). For a relatively bent CH···O interaction as in **4** [C(3)–N(3)···O: 137(5)°], a hydrogen bond length of 2.67 Å would be considered about mid-range in strength (*27*).

Experimental

Synthesis of trimethylsilylated DNA bases

The procedure follows that reported previously (*5*). A mixture of HMDS, the DNA base and a few crystals of ammonium sulphate were refluxed until the opacity of the mixture due to solid base had cleared. After the removal of the volatiles, viscous liquids remained. In the cases of cytosine, adenine and guanine, the reactions afforded crude materials that were distilled under vacuum. The distillations each yielded two products. The first, distilling at *ca.* 60°C, was found to be excess HMDS. The second was a colourless oil which solidified on cooling to give the desired silylated product. In the case of thymine, the reaction afforded a pale colourless liquid that spontaneously crystallised into the solid bis(trimethylsilyl)thymine **1**.

2–**4** were prepared similarly; experimental details are summarised in Table 6.

Crystallography

Thin, needle-like crystals of **1** and **2** were formed spontaneously from molten samples as they cooled. Crystals of **3** and **4** were grown from a saturated solution in HMDS.

Experimental details relating to the single-crystal X-ray crystallographic studies are summarised in Table 7. For all structures, data were collected on a Nonius Kappa CCD diffractometer at 150(2) K using Mo-k_α radiation ($\lambda = 0.71073$ Å). For **3** a symmetry-related (multi-scan) absorption correction was employed. Structure solution, followed by full-matrix least-squares refinement was performed using the WinGX 1.70 suite of programs throughout (*28*).

Table 5. Selected bond lengths (Å) and angles (°) for tris(trimethylsilyl)guanine (**4**).

		Guanine·H_2O[a,b]
Bond lengths		
Si(1)–O	1.665(4)	
Si(2)–N(2)	1.778(4)	
Si(3)–N(4)	1.740(4)	
C(1)–O	1.335(5)	1.239
C(1)–C(2)	1.380(7)	1.405
C(1)–N(5)	1.329(6)	1.398
C(5)–N(5)	1.353(6)	1.371
C(5)–N(4)	1.380(6)	1.333
C(5)–N(3)	1.313(6)	1.315
N(3)–C(4)	1.330(6)	1.364
C(4)–C(2)	1.392(6)	1.392
N(2)–C(4)	1.384(6)	1.364
N(2)–C(3)	1.359(7)	1.369
C(3)–N(1)	1.318(8)	1.319
N(1)–C(2)	1.373(7)	1.405
Bond angles		
Si(1)–O–C(1)	129.3(3)	
Si(3)–N(4)–C(5)	128.1(4)	
C(2)–C(1)–O	119.9(4)	127.7
N(5)–C(1)–O	119.7(4)	120.4
C(2)–C(1)–N(5)	120.4(4)	111.9
C(1)–N(5)–C(5)	117.2(4)	124.6
N(3)–C(5)–N(4)	116.5(4)	120.0
N(5)–C(5)–N(4)	114.8(4)	115.3
N(3)–C(5)–N(5)	128.7(4)	124.6
C(5)–N(3)–C(4)	111.6(4)	111.9
N(3)–C(4)–N(2)	126.8(4)	126.2
N(3)–C(4)–C(2)	126.6(4)	127.6
N(2)–C(4)–C(2)	106.5(4)	106.1
Si(2)–N(2)–C(3)	126.8(4)	
Si(2)–N(2)–C(4)	128.5(3)	
C(4)–N(2)–C(3)	104.4(4)	107.0
N(2)–C(3)–N(1)	115.1(5)	113.0
C(3)–N(1)–C(2)	103.8(4)	104.2
N(1)–C(2)–C(1)	134.4(4)	131.2
N(1)–C(2)–C(4)	110.1(4)	109.6
C(1)–C(2)–C(4)	115.5(4)	119.2

[a] Ref. (*4*).
[b] Estimated esds: 0.010–0.015 Å, 1.0–1.5°.

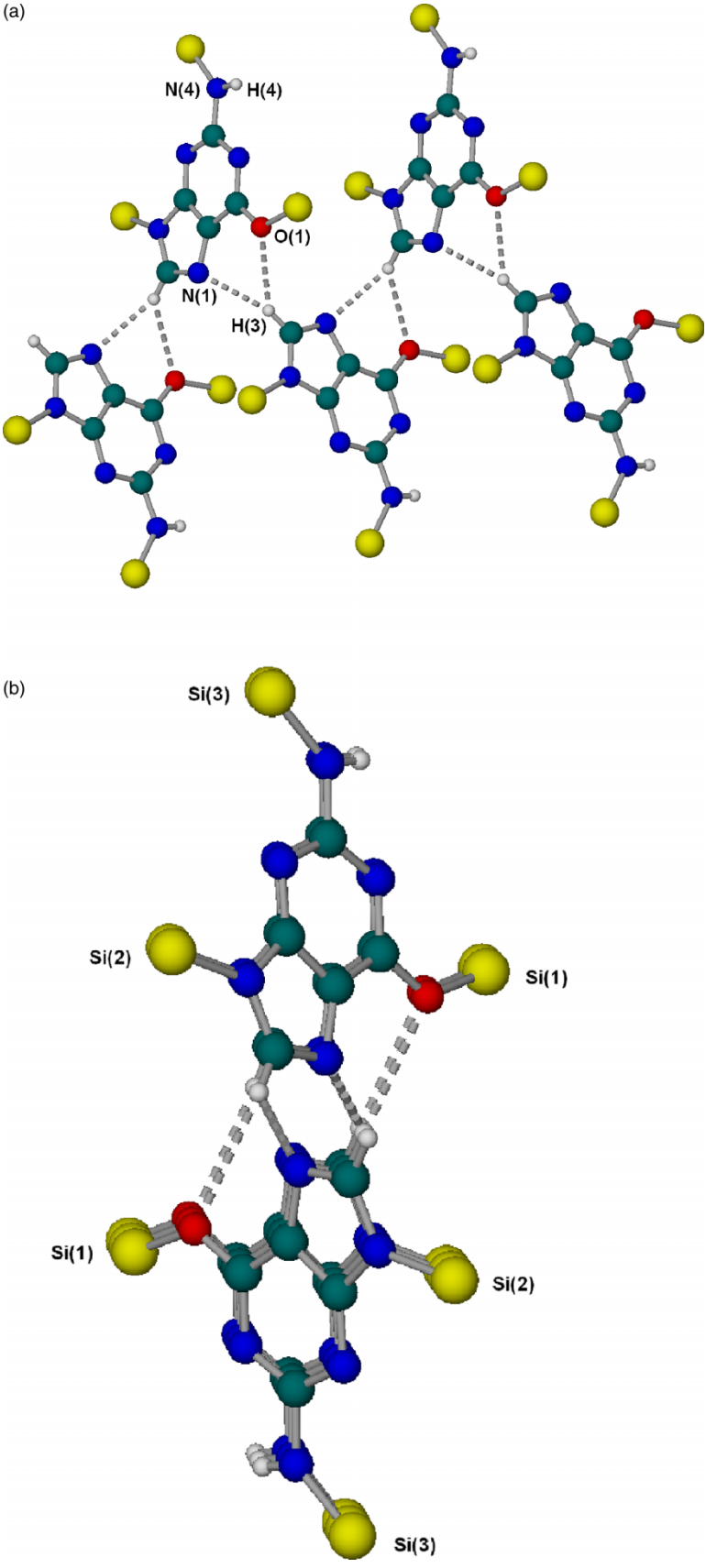

Figure 7. The lattice structure of **4** viewed (a) orthogonal to and (b) along the axis of propagation.

Table 6. Experimental data for the synthesis of trimethylsilylated DNA bases.

	Base	Time (h)	Base (g, mmol)	HMDS (cm^3, mmol)	Yield (g, %)	MP (°C)[a]	Distillation temperature[b]
1	Thymine	20	10.4, 82	20.0, 94	20.6, 93	128–130	
2	Cytosine	20	5.0, 45	28.5, 135	1.59, 20	128	200
3	Adenine	72	5.0, 37	35.0, 160	5.21, 50	130	240
4	Guanine	144	5.0, 33	21.0, 99	8.34, 72	121–123	250

[a] Reported melting points for silylated bases: **1**: 135–136°C (*5*), **2**: 122–123°C (*6*) and **3**: 84–87°C (*6*).
[b] °C/0.1 atm.

Table 7. Crystallographic data for **1**–**4**.

	1	**2**	**3**	**4**
Empirical formula	$C_{11}H_{22}N_2O_2Si_2$	$C_{10}H_{21}N_3OSi_2$	$C_{11}H_{21}N_5Si_2$	$C_{14}H_{29}N_5OSi_3$
Formula weight	270.49	255.48	279.51	367.69
Crystal system	Tetragonal	Orthorhombic	Monoclinic	Monoclinic
Space group	$P\,4_32_12$	$P2_12_12_1$	$C\,2/c$	$P\,2_1/n$
a (Å)	11.09190(10)	11.7150(3)	23.1617(6)	17.1050(5)
b (Å)	11.09190(10)	11.8760(3)	12.2279(3)	6.8600(2)
c (Å)	25.5724(4)	21.7350(7)	22.9017(7)	20.3940(7)
β (°)			97.794(2)	112.662(2)
Volume ($Å^3$)	3146.18(6)	3023.93(15)	6426.3(3)	2208.28(12)
Z	8	8	16	4
μ (Mo–K_α) (mm^{-1})	0.220	0.222	0.214	0.225
Crystal size (mm)	0.45 × 0.10 × 0.08	0.35 × 0.15 × 0.08	0.28 × 0.28 × 0.10	0.75 × 0.40 × 0.35
Theta range for data collection	3.05–26.37°	3.73–27.62°	3.76–27.60°	5.95–25.00°
Reflections collected	21,526	19,385	46,330	22,773
Independent reflections	3213 [R(int) = 0.0637]	6677 [R(int) = 0.0789]	7313 [R(int) = 0.0985]	3761 [R(int) = 0.0970]
Reflections observed (>2 σ)	2979	4810	4355	2838
Goodness of fit on F^2[a]	1.059	1.061	1.023	1.086
Final R_1[b], wR_2[c] indices [$I > 2\,\sigma(I)$]	0.0317, 0.0732	0.0451, 0.0856	0.0582, 0.1435	0.0836, 0.1864
R_1[b], wR_2[a] indices (all data)	0.0387, 0.0758	0.0859, 0.1056	0.1164, 0.1668	0.1112, 0.2144
Absolute structure parameter	0.05(11)	−0.10(12)		
Largest diff. peak, hole (e $Å^{-3}$)	0.328, −0.414	0.259, −0.357	1.031, −0.439	0.544, −0.304

[a] GOF = $S = \{\Sigma[w(F_o^2 - F_c^2)^2]/(n-p)\}^{1/2}$.
[b] $R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$.
[c] $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$.

All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included at calculated positions, except for those hydrogens involved in forming hydrogen bonding. However, in **2** one of the freely refined N—H positions had finally to be restrained to 0.87 Å because otherwise it refined to too short an N—H separation. Both **2** and **3** have asymmetric units that comprise two independent molecules.

The Cambridge Crystallographic Data Centre (CCDC) reference numbers are 658303–658306 for **1**–**4**, respectively.

Conclusions

Crystalline samples of bis(trimethylsilyl)thymine (**1**), bis(trimethylsilyl)cytosine (**2**), bis(trimethylsilyl)adenine (**3**) and tris(trimethylsilyl)guanine (**4**) have been prepared and structurally characterised by X-ray diffraction. Each showed different structural interactions in the solid state. **1** was shown to be a monomer in the solid state, having no free hydrogens for intermolecular interaction, **2** forms a polymeric chain via alternating N—H···O and N—H···N hydrogen bonds, **3** incorporates both a dimer via two N—H···N hydrogen bonds and a monomer with an intramolecular N—H···N hydrogen bond, while **4** forms a polymeric chain via unexpected bifurcated C—H···N/O hydrogen bonds leaving an available NH moiety unused.

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