Experimental Section

All new compounds were fully characterized by high-field ^{1}H and ^{13}C NMR spectroscopy and by elemental analysis or high-resolution mass spectrometry.

8: To a stirred mixture of *t*BuOH (6 mL) and water (1.5 mL) at 60 °C was added powdered KOH (3 g, 53.5 mmol). After the base had dissolved, a solution of **7** (0.367 g, 0.326 mmol) in CCl_4 (6 mL) was added, and the biphasic mixture was stirred at 60 °C for 1 h. After cooling to room temperature, the pale yellow mixture was transferred to a separating funnel and the lower aqueous layer removed. The organic phase was washed with brine and dried (Na_2SO_4), and the solvent removed in vacuo. Purification by column chromatography on silica gel (light petroleum ether/EtOAc/Et_3N 74/25/1) gave alkene **8** (0.167 g, 48 %) as a pale yellow oil. TLC: R_f = 0.36 (light petroleum ether/EtOAc 3/1); IR: $\tilde{\nu}_{max}$ (liquid film) = 1687 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.11 (1H, d, ^3J = 8.7 Hz, vinyl H); ^{13}C NMR (67.9 MHz, $CDCl_3$): δ = 68.7, 69.0, 72.1, 73.3, 73.5, 73.8, 74.2, 74.6, 74.9, 75.6, 77.9, 78.0, 78.2, 78.7, 83.1, 84.6, 86.7, 108.5 (*C*=C–O), 126.9 – 128.3 (aryl C), 137.8, 138.2, 138.3 (×2), 138.6, 138.7, 152.6 (C=*C*–O); FAB-MS: *m*/*z*: 1081 [*M*+Na$^+$].

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Charge Transfer and Environment Effects Responsible for Characteristics of DNA Base Pairing**

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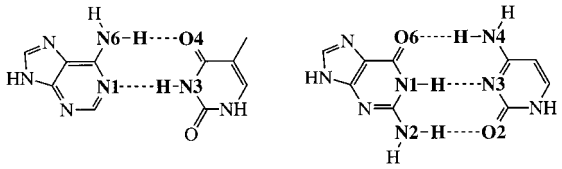
Although it is one of the weakest chemical interactions the hydrogen bond plays a key role in the chemistry of life, being involved, for example, in various types of self-organization and molecular recognition. A case in point is the hydrogen bonds in Watson – Crick base pairs, that is, adenine – thymine (AT) and guanine – cytosine (GC), that hold together the two helical chains of nucleotides in DNA and form the basis of the genetic code. These hydrogen bonds are commonly believed



AT GC

to be predominantly electrostatic phenomena that, as suggested by Gilli et al., are substantially reinforced by resonance in the π-electron system, which makes the proton-acceptor atom more negative and the proton-donor atom more positive the so-called resonance-assisted hydrogen bonding (RAHB).[1]

Herein we provide evidence from quantum chemical analyses that challenges this picture and emphasizes the importance of the charge-transfer nature of and environment effects on the hydrogen bonds in DNA base pairs. This has led us to the solution of a hitherto unresolved and significant discrepancy between experimental[2] and theoretical[3] values for distances between the proton-donor and proton-acceptor atoms in AT and GC base pairs. Our evidence is based on a thorough nonlocal density functional theoretical (DFT) investigation with the ADF program (at BP86/TZ2P) of various AT and GC model systems.[4, 5]

Whereas our base-pairing enthalpies (298 K, BSSE corrected) of −11.8 and −23.8 kcal mol^{-1} for AT and GC, respectively, are in excellent agreement with gas-phase experimental values (−12.1 and −21.0 kcal mol^{-1}),[6] we still arrive at the same striking discrepancies with experimental (X-ray crystal) structures[2] that were encountered before in conventional ab initio (HF) and hybrid DFT (B3LYP) studies.[3] As shown in Figure 1 we find N6–O4 and N1–N3

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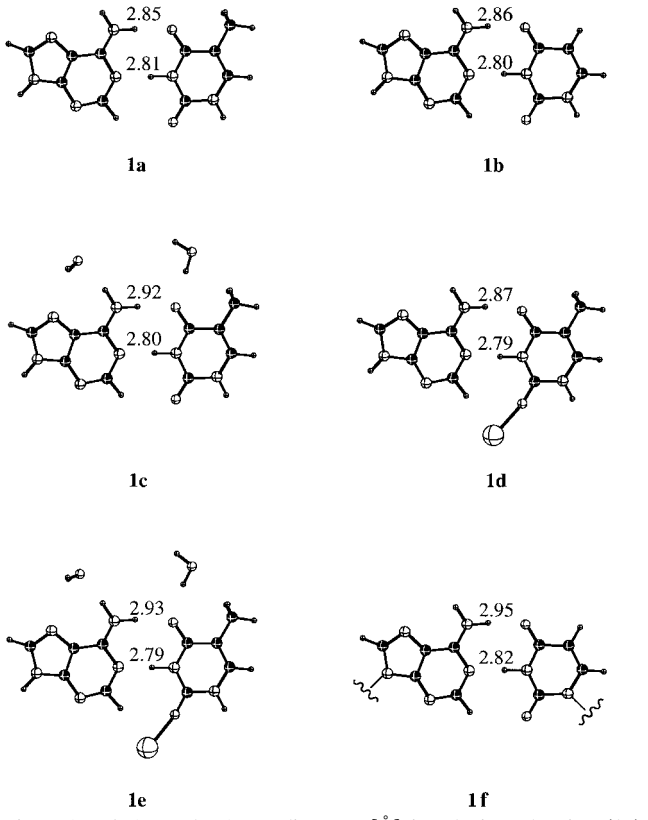

Figure 1. N6–O4 and N1–N3 distances [Å] in adenine–thymine (**1a**), adenine–uracil (**1b**), and various AT model systems containing water molecules and/or a sodium ion (**1c–e**) determined from BP86/TZ2P computations, as well as in the crystal of sodium adenylyl-3′,5′-uridine hexahydrate as determined from an X-ray diffraction study (**1f**).[2b]

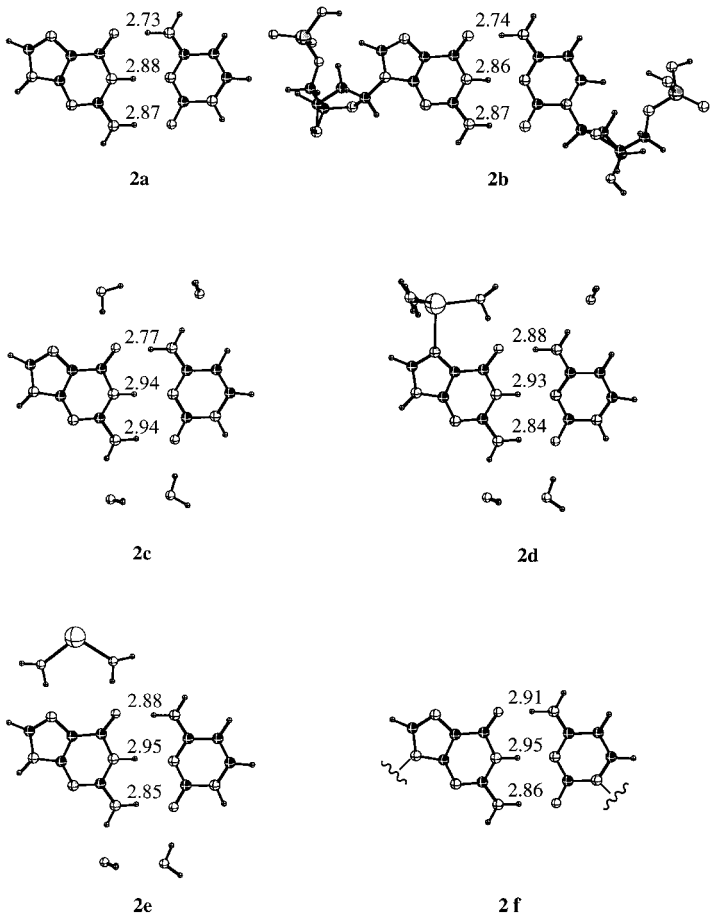

Figure 2. O6–N4, N1–N3, and N2–O2 distances [Å] in guanine–cytosine (**2a**), in the nucleotide pair dGMP–dCMP with inclusion of the backbone (**2b**), and various GC model systems containing water molecules and/or a sodium ion (**2c–e**) determined from BP86/TZ2P (**2a, 2c–e**) and BP86/DZP (**2b**) computations, as well as in the crystal of sodium guanylyl-3′,5′-cytidine nonahydrate as determined by an X-ray diffraction study (**2f**).[2c]

hydrogen-bond lengths in AT of 2.85 and 2.81 Å, respectively, (**1a**) which are essentially equal to those in AU (**1b**). These values have to be compared with 2.95 and 2.82 Å from experiment (**1f**). Even more eye-catching is the situation for the three hydrogen bonds in GC (Figure 2), namely O6–N4, N1–N3, and N2–O2, for which we find a bond length pattern that is short-long-long (2.73, 2.88, and 2.87 Å, **2a**), which is significantly different from the experimental values that are long-long-short (2.91, 2.95, and 2.86 Å, **2f**). We have verified that these inconsistencies are not induced by our neglecting the glycosidic N–C bond. Methylation of the bases at N9 (adenine or guanine) or N1 (thymine or cytosine), for example, which is a way to mimic the glycosidic N–C bond, has basically no effect on the hydrogen bonds in AT and GC base pairs: hydrogen-bond energies (zero K, no BSSE correction) differ by 0.0 and 0.3 kcal mol^{-1}, respectively, and the largest change in hydrogen-bond lengths amounts to 0.01 Å at BP86/TZ2P (not shown in the figure). Likewise, the hydrogen-bond lengths of the GC pair consisting of nucleotides (**2b**, Figure 2) differ only slightly from those in the plain GC pair (**2a**), that is, by 0.02 Å or less at BP86/DZP.

To trace the origin of the discrepancy between quantum chemical and experimental structures we have analyzed the A–T and G–C interactions of C_s-symmetric base pairs (whose hydrogen bonds differ by less than 0.005 Å and 0.1 kcal mol^{-1} from those of the C_1 symmetric **1a** and **2a**) in the conceptual framework provided by the Kohn–Sham molecular orbital (KS-MO) model through a decomposition of the actual interaction energy (ΔE_{int}) into the classical electrostatic interaction (ΔV_{elst}), the attractive orbital interactions comprising charge transfer and polarization (ΔE_{oi}), and the Pauli repulsive orbital interactions between closed shells (ΔE_{Pauli}).[5] It appears that in both DNA base pairs, AT and GC, the bonding orbital interactions associated with hydrogen bonding are of comparable magnitude as the electrostatic attraction (for AT ΔE_{oi} and ΔV_{elst} are -22.4 and -32.1 kcal mol^{-1}, respectively, and for GC -34.1 and -48.6 kcal mol^{-1}, respectively). A more detailed examination of ΔE_{oi} and the associated changes in the wavefunction (orbital mixings) shows that the hydrogen-bonding orbital interactions are predominantly provided by charge-transfer interactions in the σ-electron system between a lone pair on a nitrogen or oxygen atom on one base and the N–H σ*-cceptor orbitals of the other base. Figure 3 shows the relevant frontier-orbital interactions for AT that emerge from our Kohn–Sham MO analysis (a similar diagram can be drawn for GC). Indeed, we do find orbital interactions in the π-electron system that are reminiscent of the RAHB model: by polarization of the π-charge distribution within a DNA base they compensate the build-up of charge caused by charge-transfer hydrogen

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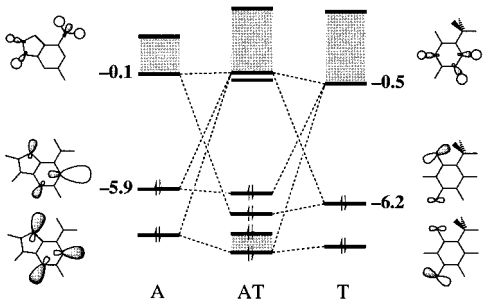

Figure 3. Frontier orbital interactions between adenine and thymine in AT (**1a**) from BP86/TZ2P Kohn–Sham DFT analyses (the base HOMO and LUMO energies of the σ-electron systems are given in eV). The group of lowest unoccupied orbitals involved is represented by a block.

bonding in the σ-electron system. The corresponding π interaction amounts to -1.7 and -4.8 kcal mol^{-1} for AT and GC, respectively, that is, only 3 and 6% of the total attractive interactions $\Delta E_{oi}+\Delta V_{elst}$. In that respect π assistance is of minor importance. On the other hand the π interactions contribute 14–20% of the net bond enthalpies and, on the very shallow potential energy surface they are able to bring about a shortening of the hydrogen bonds by 0.1 Å. In this sense one may speak of a certain π assistance, despite this term being rather small compared to the charge-transfer and electrostatic interactions.

Additional support for charge transfer comes from an analysis of the deformation density $\rho_{pair}(r)-\rho_{base\,1}(r)-\rho_{base\,2}(r)$, that is, the redistribution of charge density that is caused by the formation of a DNA base pair from its constituting bases. This can be quantified by using an extension of the Voronoi deformation density (VDD) method,[7] in which the change in atomic charges associated with base pairing ΔQ_A is defined and related to the deformation density by Equation (1), where VVA means the volume of the Voronoi cell of atom A in the base pair.

$$\Delta Q_A^{VDD} = -\int_{VVA} [\rho_{pair}(r)-\rho_{base\,1}(r)-\rho_{base2}(r)]\,dr \qquad (1)$$

The interpretation of VDD atomic charges is rather straightforward. Instead of measuring the amount of charge associated with a particular atom A, they directly monitor how much charge flows, as a result of chemical interactions between DNA bases, out of ($\Delta Q_A > 0$) or into ($\Delta Q_A < 0$) the Voronoi cell of atom A, that is, the region of space that is closer to nucleus A than to any other nucleus. We have verified that all VDD values are stable with respect to variations of the basis by computing the VDD charges at BP86 with three different Slater-type basis sets, namely, DZ (unpolarized double-ζ), DZP (singly polarized double-ζ), and TZ2P (doubly polarized triple-ζ): the maximum deviation is 0.01 electrons. This affects neither the physical picture nor our conclusions. Full details of our analyses will be published elsewhere.

The donor–acceptor interaction in AT associated with the hydrogen bond N1···H–N3 (involving two donating adenine orbitals with N1 lone-pair character) leads to a net transfer of 0.05 electrons from A to T (computed with σ virtuals on T only and all other virtuals removed). This is counteracted by a transfer of 0.04 electrons back from T to A as a consequence of the hydrogen bond N6–H···O4 (involving one donating thymine orbital with O4 lone-pair character), which leads to a slight build-up of negative charge on thymine. Likewise, for the GC pair, we find a build-up of negative charge on guanine that stems from a transfer of 0.05 electrons from G (with one lone pair donating atom, O6) to C through hydrogen bond O6···H–N4 that is outweighed by the transfer of 0.07 electrons back from C (with two donating atoms, N3 and O2) to G through the two hydrogen bonds N1–H···N3 and N2–H···O2.

The simultaneous occurrence of hydrogen bonds that donate charge in opposite directions reduces the net build-up of charge on the DNA bases, and one might thus expect that these hydrogen bonds reinforce each other. However, the corresponding analysis of the bond energy shows that there is no such synergism. The deformation density (not shown here) reveals that this is so because each hydrogen bond creates its own local charge separation that is not affected by the occurrence of another hydrogen bond.

It appears from a breakdown of the VDD charges into contributions from the σ-end π-electron system ($\Delta Q_A = \Delta Q_A^{\sigma} + \Delta Q_A^{\pi}$) that virtually all charge transfer occurs in σ symmetry. The ΔQ_A^{π} values reveal that the π system of each individual DNA base polarizes in such a way that the accumulation of positive or negative charge around the donating or accepting atoms, caused by the charge transfer in the σ-electron system, is counteracted and partly relieved. However, we do not find any synergism between ΔE_{σ} and ΔE_{π}, that is, ΔE_{σ} is not increased by the occurrence of the π-electron polarization.

The extremely shallow potential-energy surface that we find for the hydrogen bonds in DNA base pairs makes it plausible that the structure of AT and GC in the crystal or under physiological conditions is significantly influenced by interactions with the environment, such as, hydration, coordination of alkali metal ions (Na^+), and hydrogen bonding to hydroxyl groups of the sugar. Therefore, we have tried to simulate the major environmental effects that occur in the crystals used in the experimental X-ray structure determinations of AT and GC, namely, the crystal of sodium adenylyl-3′,5′-uridine hexahydrate (ApU hexahydrate, **1f**)[2b] and that of sodium guanylyl-3′,5′-cytidine nonahydrate (GpC nonahydrate, **2f**).[2c] And indeed, as can be seen from Figures 1 and 2, the addition of water molecules (simulating a part of the hydration and hydrogen bonding with ribose OH groups) and the introduction of the sodium counterions along **1a–e** and **2a–e** deforms the geometry of AT and GC in such a way that excellent agreement between our DFT model (for example, **1e**: N6–O4 and N1–N3 are 2.93 and 2.79 Å, respectively; **2e**: O6–N4, N1–N3, and N2–O2 are 2.88, 2.95, and 2.85 Å, respectively) and the experimental structures is obtained. Our results show that present-day approximate DFT not only provides a highly efficient but, if appropriate model systems are chosen, also a suitable and accurate alley towards describing and understanding hydrogen bonding in DNA base pairs.

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Stereoselective Synthesis of Coordination Compounds: Self-Assembly of a Polymeric Double Helix with Controlled Chirality**

Olimpia Mamula, Alex von Zelewsky,* Thomas Bark, and Gérald Bernardinelli

The formation of helical structures by the assembly of metal coordination species has received a great deal of attention in recent years. The field of helicates has recently been reviewed by Piguet et al.,[1] and several observations of infinite coordination helices have been reported.[2–13] Most of these infinite helices are formed from achiral ligands,[2–9] consequently yielding racemates of *P* and *M* helices. In a few cases chiral predetermination is achieved by the use of enantiopure ligands.[10–13]

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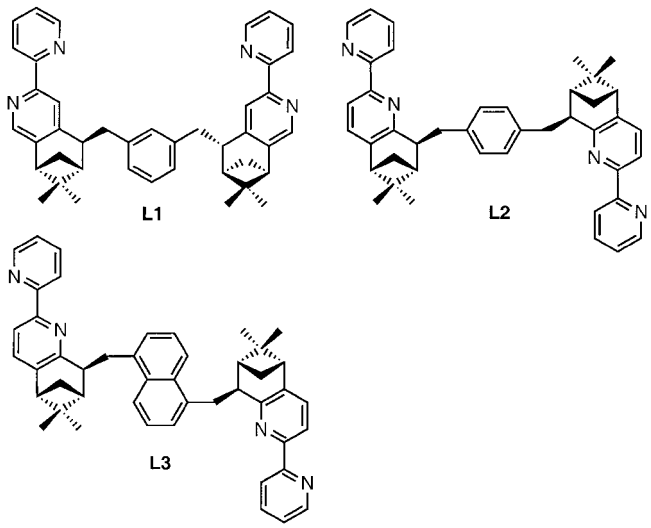
Here we describe a self-assembled coordination polymer that is chirally predetermined and represents, to the best of our knowledge, the first example for intertwining of two single-stranded helicates to form an infinite, highly symmetric double helix. The two strands of this double helix are connected neither by chemical bonds nor through attractive intermolecular forces, except unspecific van der Waals interactions.

We have shown recently that CHIRAGEN-type ligands[14] can give rise to the formation of self-assembled helicates that are predetermined in their chirality. With metals that give octahedral coordination, 4,5-CHIRAGEN[*m*-xylyl] (**L1**) yields dinuclear species of M_2L_3 stoichiometry.[15] This 2:3 stoichiometry seems to be fairly common, since several other ligands in which two bidentate units are connected through a bridge provide such assemblies.[1, 16–19] The use of the 5,6-CHIRAGEN **L2** containing a *para*-xylylidene bridge with



metals that form tetrahedral coordination species, such as Ag^+ and Cu^+, yielded highly symmetric, circular, hexanuclear single-stranded helicates; the chirality is again totally predetermined by the chiral pinene groups present in these ligands.[20] To investigate further the influence of the ligand geometry on the molecular assembly, we varied the bridge in the 5,6-CHIRAGEN ligand. Here we report the structural properties of the species obtained with the ligand **L3**, in which the bridge has been derived from 1,5-dimethylnaphthalene.

The ligand **L3** was synthesized following the general procedure (Scheme 1) that has been applied for several other ligands of the CHIRAGEN family.[14, 21, 22] The ligand was completely characterized, and its NMR spectra show the symmetry expected owing to the C_2 axis perpendicular to the naphthalene plane and passing through its center. As a consequence of the high stereoselectivity in its synthesis, the ligand is isomerically pure within NMR analytical accuracy. According to the NMR spectra, a self-assembled species with high symmetry is formed upon addition of Ag^+, as in the case of **L2**.[20] Figure 1 shows the aromatic part of the ^1H NMR spectra of the free ligand **L3** (b) and of the silver complex (a).

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