Watson–Crick pairing of nucleobases functionalized with open-shell molecular entities in crystalline solids†

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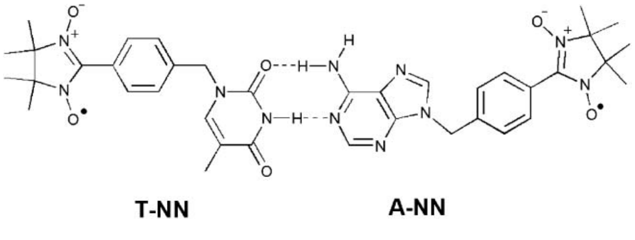
A Watson–Crick type molecular complex of adenine and thymine bases substituted with the stable radical of nitronylnitroxide has been synthesized, which forms a double-chain spin system in the crystal.

The control of molecular packing in the crystalline solid state is the focus of the current issues in developing exotic molecule-based magnetic materials,[1] because magnetic properties of molecular assemblages are governed by spatial arrangements of constituent open-shell molecules in the crystalline solid. Utilization of intermolecular hydrogen bonding[2] is one of the promising strategies for controlling the arrangement of open-shell entities in the crystal.[3] Nucleobases such as guanine, cytosine, adenine and thymine constituting a DNA duplex are fascinating building blocks as they can form complementary hydrogen bonds with high selectivity and directionality. Several examples have been found in which stable radicals of nitroxide are introduced to nucleobases in crystalline solid states,[4] while solution chemistry and ESR spectroscopy have been reported for spin-labeled nucleosides and nucleotides,[5,6] and for nucleobase-substituted tetrathiafulvalene (TTF) analogues and TTF-based cation radicals.[7]

In this study, we extend the hydrogen-bonded radical-substituted nucleobase systems to heteromolecular complexes with complementary base pairing. We report for the first time the synthesis and X-ray structural characterization of a heteromolecular complex of nucleobases possessing stable organic radical moieties on both sites of the complementary pair. The constituent molecules are nitronylnitroxide (NN) radicals substituted with adenine (**A-NN**) and thymine (**T-NN**), as shown in Scheme 1. Magnetic properties of the crystalline aggregate of the A–T complex are interpreted in terms of the molecular packing whose mode is governed by the complementary hydrogen bonding of the nucleobases.



Scheme 1 Nitronylnitroxide-substituted nucleobases.

A-NN and **T-NN** were synthesized from a *p*-bromomethylphenyl derivative of nitronylnitroxide and adenine or thymine.‡ Single crystals of the complex were obtained by recrystallization from chloroform and hexane solutions.§

From X-ray crystallography, the adenine and thymine moieties are found to form a reverse Watson–Crick pair (Fig. 1) with two-fold hydrogen bonds, N7H21–O6 and N11H42–N5. The purine and pyrimidine planes are twisted to each other by 11.1(1)°. Both the dihedral angle and the hydrogen bond lengths (N7H21–O6 = 3.088(3) Å, N11H42–N5 = 2.799(3) Å) fall within the typical values of reverse Watson–Crick pairs of previously studied adenine–pyrimidine base complexes as examined by X-ray single-crystal structure analyses.[8] Between the base pairs the neighboring adenine moieties are related by a center of symmetry (*i*: $2 - x$, $-y$, $2 - z$) and form hydrogen bonds between the amino and the imidazole nitrogen atoms (N7H22–N6*i* = 3.003(4) Å). The amino–imidazole hydrogen bonding has been found as well in analogous adenine derivatives.[8,9]

The adenine–adenine and adenine–thymine hydrogen bonds govern the molecular packing of the constituent molecules of the complex, resulting in a double-chain structure of the radical fragments running along the *a–b* direction, as depicted in Fig. 2(a). Magneto-structural correlation of the chain is interpreted in the light of intermolecular short distances close to the van der Waals contact.[10] In the chain, three kinds of short contacts are found around the nitronylnitroxide groups with large spin density, which contribute to possible intermolecular exchange interactions. One of the short contacts (contact I) is found between the nitroxide oxygen atoms of **A-NN** and **T-NN** (O2–O3 = 3.184(3) Å). This contact leads to a SOMO–SOMO overlap (SOMO: singly occupied molecular orbital) between the molecules and a sizable antiferromagnetic interaction is expected. The second contact (II) is found between two inversion-related molecules of **T-NN** at C31–C29*i* of

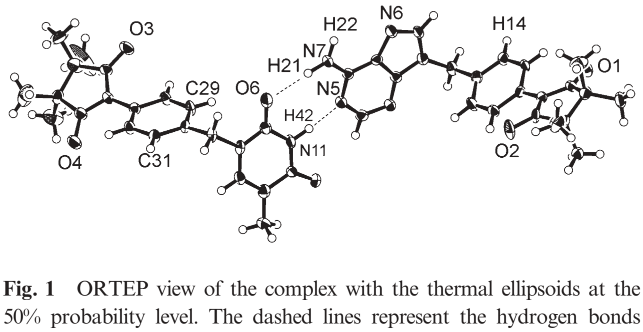


Fig. 1 ORTEP view of the complex with the thermal ellipsoids at the 50% probability level. The dashed lines represent the hydrogen bonds (N7H21–O6 = 3.088(3) Å, N11H42–N5 = 2.799(3) Å).

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† Electronic supplementary information (ESI) available: Results of DFT molecular orbital calculations. See DOI: 10.1039/b611236f

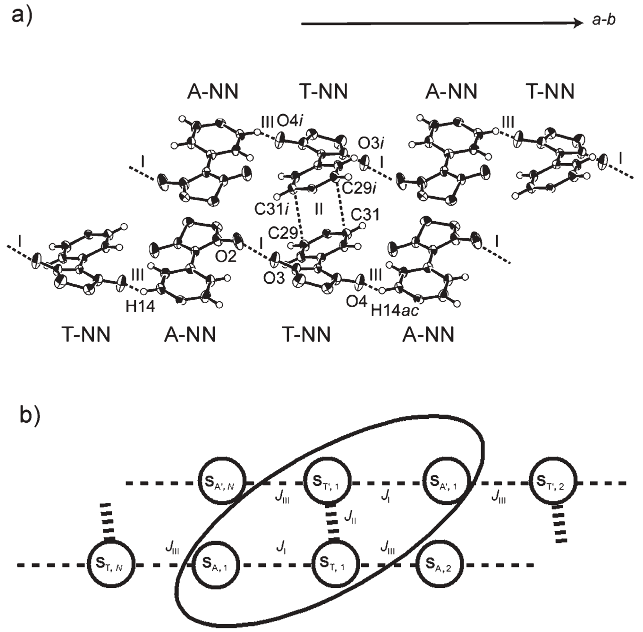

Fig. 2 (a) Molecular chain of the complex running along the *a–b* axis. The dashed lines represent the intermolecular short contacts. The nucleobase entities and the methyl groups of nitronylnitroxide are omitted for clarity. (b) Schematic drawing of the exchange coupling in the double-chain system. The circles indicate the $S = 1/2$ spins. The oval represents the repeating unit of eqn (1). S_T and S_A denote $S = 1/2$ spins of **T-NN** and **A-NN**, respectively.

3.566(5) Å. The third contact (III) is between the nitroxide oxygen atom (O4) of **T-NN** and the hydrogen atom (H14) of **A-NN** neighboring along the chain axis (*ac*: $x - 1, y + 1, z - 1$; O4–H14*ac* = 2.566 Å). This side-by-side contact is expected to give a ferromagnetic exchange interaction between phenylnitronylnitroxide molecules, as found in other nitronylnitroxide crystals.[11]

It is found from DFT molecular orbital calculations that the spin density of the adenine and thymine entities in **A-NN** and **T-NN** is much smaller than that of nitronylnitroxide moieties by three orders of magnitude,[12] indicating that the nucleobase moieties play a primary role in determining the molecular packing instead of propagating intermolecular magnetic interactions. Thus, exchange interactions through the hydrogen bond within the nucleobase pair can be neglected to the first approximation and the exchange-coupled spin system of the complex is approximated by a double-chain structure as shown in Fig. 2(b). The intermolecular exchange interactions originating from the contacts at O2–O3 (I), C31–C29*i* (II) and O4–H14*ac* (III) are labeled $J_{\rm I}$, $J_{\rm II}$ and $J_{\rm III}$, respectively.

The temperature dependence of paramagnetic susceptibility $\chi_{\rm p}$ for the polycrystalline sample of the complex is shown in Fig. 3 for the $\chi_{\rm p}T$ *versus* T plots. The $\chi_{\rm p}T$ value of 0.74 emu mol^{-1} K at room temperature corresponds to two moles of $S = 1/2$ spins. Upon cooling, the $\chi_{\rm p}T$ value decreases. The temperature dependence of $\chi_{\rm p}T$ is analyzed using the effective exchange spin Hamiltonian

$$H = \sum_{i=1}^{N} [-2J_{\rm I}(S_{{\rm A},i}S_{{\rm T},i} + S_{{\rm A}',i}S_{{\rm T}',i}) - 2J_{\rm II}(S_{{\rm T},i}S_{{\rm T}',i}) - 2J_{\rm III}(S_{{\rm A}',i}S_{{\rm T}',i+1} + S_{{\rm T},i}S_{{\rm A},i+1})] \qquad (1)$$

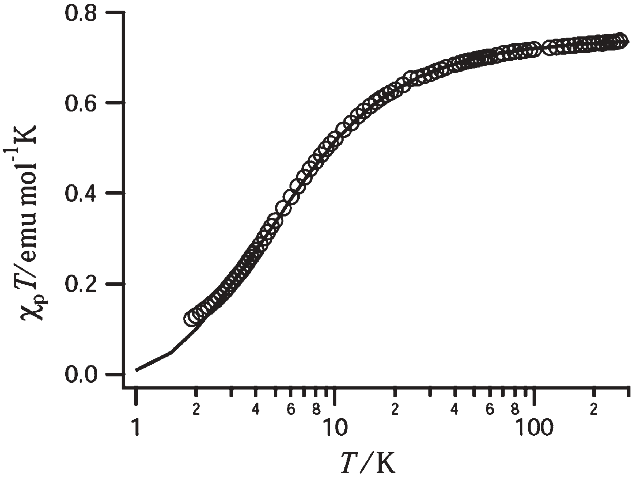

Fig. 3 Temperature dependence of the product $\chi_{\rm p}T$ measured at 0.1 T for the complex (circles). The solid line represents the theoretical calculations based on eqns (1) and (2).

where $\mathbf{S}_{{\rm A},i}$ and $\mathbf{S}_{{\rm T},i}$ denote the $S = 1/2$ spin operators of **A-NN** and **T-NN** in the *i*th unit cell of N repeating units in the double-chain structure. The Hamiltonian was numerically diagonalized to give energy eigenvalues E_j, from which the temperature dependence of $\chi_{\rm p}T$ was calculated by the following expression,

$$\chi_{\rm A} = \frac{1}{2N}\frac{\alpha N_{\rm A} g^2 \mu_{\rm B}^2}{3k_{\rm B}T}\frac{\sum_j \left[S_j(S_j+1)(2S_j+1)\exp\left(-E_j/k_{\rm B}T\right)\right]}{\sum_j \left[(2S_j+1)\exp\left(-E_j/k_{\rm B}T\right)\right]} \qquad (2)$$

The parameter α in eqn (2) denotes the purity of the sample. The symbols $N_{\rm A}$, g, $\mu_{\rm B}$ and $k_{\rm B}$ stand for Avogadro constant, the *g*-factor, Bohr magneton and Boltzmann constant, respectively. In the calculations of eqns (1) and (2), periodic boundary condition is imposed for $4N = 16$ of $S = 1/2$ spins. The solid curve in Fig. 3 represents the calculation using the best-fit parameters, $J_{\rm I}/k_{\rm B} = -4.1 \pm 0.1$ K, $J_{\rm II}/k_{\rm B} = -4.6 \pm 0.2$ K, $J_{\rm III}/k_{\rm B} = 0$ K[13,14] and $\alpha = 0.98$. The *g*-factor was fixed as $g = 2.006$, which has been obtained from the ESR spectra of **A-NN** and **T-NN** in CH_2Cl_2 solutions at room temperature. The poor fitting below 3 K is attributable to the influence of paramagnetic impurities or possible weak exchange interactions between the double-chain structures neglected in the calculation model of eqns (1) and (2).

In summary, we have prepared for the first time a reverse Watson–Crick base pair, in which stable organic radical entities are introduced onto both sites of the complementary nucleobases. The molecular packing of the complex features in intermolecular hydrogen bonds between the nucleobase substituents gives a double-chain spin system in the crystal. The solid-state magnetism of the complex has been well explained by the double-chain model with the periodic four-spin cluster. Heteromolecular aggregation based on complementary pairing of radical-substituted nucleobases will lead to exotic spin systems such as a genuinely organic molecule-based ferrimagnet.[16]

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Notes and references

‡ Synthesis: A mixture of adenine (82.8 mg, 0.61 mmol), K_2CO_3 (84.7 mg, 0.61 mmol), KI (101 mg, 0.61 mmol) and 4-(bromomethyl)phenyl nitronylnitroxide (200 mg, 0.61 mmol) in CH_3CN (5 mL) under argon were stirred at 90 °C for 4 h. The solution was extracted with CH_2Cl_2, washed with brine, and dried over $MgSO_4$. The solvent was evaporated and chromatographed over a short column (silica gel). Elution with a solution of CH_2Cl_2–MeOH (9 : 1 in volume) followed by removal of the solvent *in vacuo* gave a pure blue product (37 mg, 16%). Elemental analysis (C, H, N) Anal. Calc. for $C_{19}H_{22}N_7O_2$: C, 59.99; H, 5.83; N, 25.77%. Found: C, 59.57; H, 5.78; N, 25.22%. **T-NN** was synthesized by the same procedure as **A-NN**. Elemental analysis (C, H, N) Anal. Calc. for $C_{19}H_{23}N_4O_4\cdot 1/4H_2O$: C, 60.71; H, 6.30; N, 14.90%. Found: C, 60.89; H, 6.31; N, 14.51%.

§ *Crystal data:* The crystal structure was solved by direct methods in a program package *CrystalStructure* (version 3.70) from Rigaku/Molecular Structure Corporation, 9009 New Trails Dr. The Woodlands TX 77381 USA. Crystallographic data for $C_{38}H_{45}N_{11}O_6$: $M = 751.84$, 0.40 × 0.25 × 0.10 mm^3, MoKα, 128 K, triclinic, P-1, $a = 11.949(1)$ Å, $b = 12.850(1)$ Å, $c = 14.821(2)$ Å, $\alpha = 69.34(2)°$, $\beta = 77.56(2)°$, $\gamma = 61.72(1)°$, $V = 1872.0(3)$ Å^3, $Z = 2$, $D_{calc} = 1.334$, $R_1 = 0.091$, $R_w = 0.183$ optimised on F^2 (GOF = 1.000) for 8101 reflections (all data) and 541 parameters. CCDC 611166. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b611236f

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13 The parameter J_{III} was allowed to increase up to $J_{III}/k_B = 0.5$ K. J_{III} values in the range of $J_{III}/k_B = 0 \sim 0.5$ K gave almost identical values of $\chi_P T$ *versus* T curve. Further increase in J_{III} beyond 0.5 K or negative J_{III} results in apparent deviation from the observed values of $\chi_P T$, which is not repaired by re-optimizing J_I and J_{II}. For determing J_{III}, ultralow temperature experiments of magnetic susceptibility are necessary.

14 The double-chain model is reduced to a simpler 4-spin system when J_{III} is set to zero. For the 4-spin system, an exact solution of eigenenergies E_j's has been known (ref. 15). The 4-spin model reproduces, as expected, the magnetic susceptibility with the same fitting parameters of J_I and J_{II} as used in the chain model.

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