Multiple Hydrogen Bonding Network: A Novel Mode of Self-Recognition in a Layered Crystalline Structure of a Guanosine Derivative

Koji Araki,* Masanori Abe, Akira Ishizaki, and Tsutomu Ohya
Institute of Industrial Science, University of Tokyo, 7-22-1 Roppongi, Minato-ku, Tokyo 106

(Received December 26, 1994)

A lamella-like layered structure of the nucleoside derivative was formed by *tert*-butyldimethylsilylation of the ribose hydroxy groups upon recrystallization from methanol, in which a novel mode of self-recognition of the guanine unit by multiple hydrogen bonding interaction plays an essential role to stabilize the crystal structure.

Nucleic acid bases have multiple hydrogen-bonding sites to form hydrogen bonds within their ring plane. Complementary base pairs that are essential for the function of DNA are formed by multiple hydrogen bonding interaction, and co-planar structure of the complementary base pairs is essential to construct double helix structure of DNA. Recently, many efforts have been focused on controlling supramolecular and crystal structures of self-assembly of organic compounds by tuning hydrogen bonding interaction.[1-4] Nucleic acid bases and nucleosides are the suitable substrates for construction of an organized structure by multiple hydrogen bonding interaction. Here, we wish to report a lamella-like layer crystalline structure of a guanosine derivative, in which multiple hydrogen bonding network formed by a novel mode of self-recognition between the base moieties contributed to stabilize the structure.

The ribose moiety of nucleosides has hydroxy groups that might participate in hydrogen bonding interaction between the base moieties, causing difficulty in controlling inter-nucleoside hydrogen bonding interaction. In this study, we adopted a novel approach to control the hydrogen bonding interaction between nucleoside. It is well known that amphiphilic surfactants and lipids form variety of self-organized structures by spontaneous aggregation of polar head groups and nonpolar alkyl chain separately.[5] Trialkylsilylation of the hydroxy groups alters polar nature of the ribose moiety into nonpolar one, giving amphiphilic nature to the nucleoside derivative. Unlike electrostatic interaction, multiple hydrogen bonding interaction requires strict spatial arrangement of the base moieties. Therefore, alkylsilyl chain that has high flexibility and low polarity[6] is a suitable unit for construction of an organized self-assembly.

Based on the above concept, we prepared 2',3',5'-tris(*t*-butyldimethylsilyl)guanosine (TBDMS-G) according to the method described in a literature.[7] The compound yielded a rectangular granule on recrystallization from methanol. The crystal cropped freshly from methanol was transparent, and structural analysis was carried out by X-ray crystallography (R=0.071).[8]

The crystal was an orthorhombic with a unit cell dimension of 19.4 x 33.5 x 12.9 Å. The base moiety and the TBDMS unit of TBDMS-G compose separate layers, and the base layer is sandwiched by the TBDMS layers (Figure 1). Two methanol molecules per TBDMS-G are incorporated in the crystal, which are located in the base layer. Within the base layer, two intermolecular hydrogen bonds are formed between adjacent guanine moieties. One is between 3-NH_2 and 6-C=O, and the other between 1-NH and 7-N through the hydroxy group of

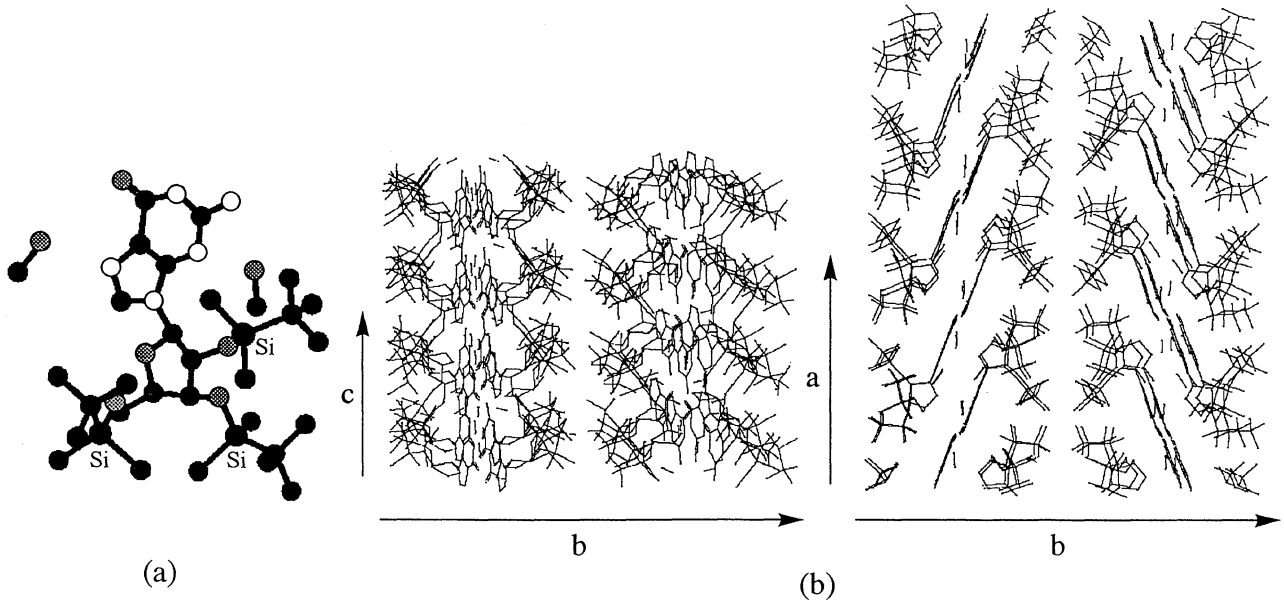

Figure 1. (a) Molecular and (b) Crystal Structure (Orthorhombic, B2212(#20), Unit cell: a=19.369, b=33.473, and c=12.879 Å) of TBDMS-Guanosine (R=0.071, Rw=0.066).

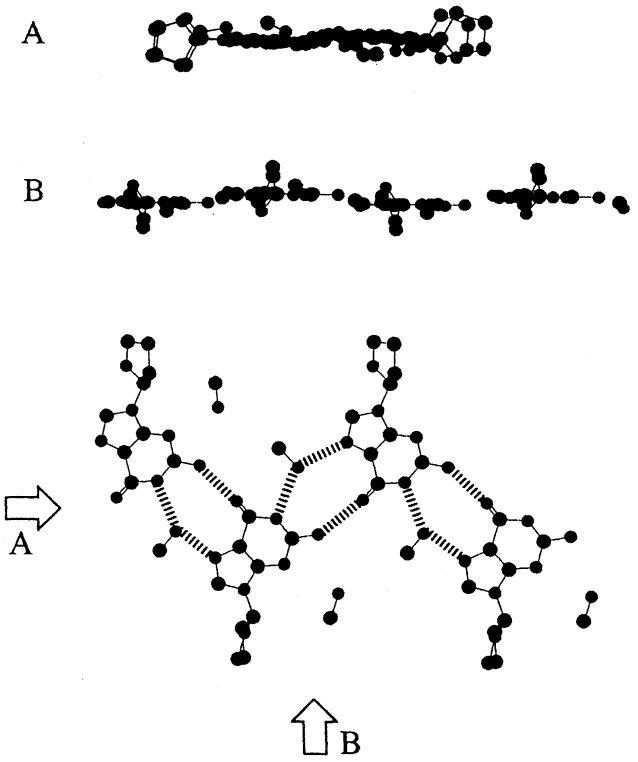

Figure 2. Hydrogen Bonding Network between the Guanine Moieties of TBDMS-Guanosine through Methanol.

methanol (Figure 2). The double hydrogen bond network stretches through the guanine moieties to fix them in a same plane, and the base planes are lined side by side with aslant to form the base layer. This is a novel mode of self-recognition between the guanine unit by multiple hydrogen bonding interaction. As the guanine moiety is not located on the top of other guanine moieties in the adjacent planes, direct π-π stacking interaction between the base moieties is unlikely to occur. Though one methanol molecule in the crystal participates in the hydrogen bond network, the other methanol is not involved in the network but is hydrogen-bonded to the ring nitrogen at 3 position. Nonpolar TBDMS layers sandwiched the base layer to form the layer-type assembly, which has close resemblance to the lamellar structure of the lipids or surfactants.

Though freshly obtained crystal was colorless and transparent, it gradually turned to white in the air. DSC curve of the sample during the first heating process showed large endothermic peak up to 80°C presumably due to evaporation of methanol. Decrease of the crystal weight during this process corresponded to loss of one methanol molecule per TBDMS-G in the crystal. Another small endothermic peak was observed at 86°C without any weight loss, and repeated heating of the sample up to 120°C showed only the reproducible endothermic peak at 85-88°C. Since melting point of t-butyldimethylsilyl chloride is 86-89°C, the endothermic peak observed at 85-88 °C of the crystal is ascribed to the melting of the t-butyldimethylsilyl moieties of TBDMS-G. It is worth noting that the other methanol was retained in the crystal even after heated at 120°C.

The sample heated at 120°C retained its original shape. Though X-ray crystallographic analysis did not give clear structure of the heated sample, powder X-ray diffraction pattern showed the peaks corresponding to the spacing of the unit cell of the original crystal, showing that the original crystal structure was preserved after heating. Thus, it is demonstrated that the hydrogen-bond network between the guanine unit through methanol is stable enough even above the melting point of the TBDMS units, though the other methanol that is not involved in the network is lost readily by heating.

In conclusion, introduction of nonpolar and flexible TBDMS units to the ribose hydroxy groups resulted in formation of a novel lamella-like layered structure, in which the novel mode of self-recognition between the guanine moieties by multiple hydrogen bonding interaction plays an essential role to stabilize the organized structure. It is likely that participation of methanol in the hydrogen bonding network allows appropriate arrangement of the base moieties to fit with the size of the TBDMS-unit.[9] Currently we are studying the effect of different mode of recognition between base pairs and/or size of nonpolar unit on the organized structure of the nucleoside derivatives.

We thank Prof. K.Saigo, Faculty of Engineering, University of Tokyo, for X-ray crystallographic measurement. This work was partly supported by a Grant-in-Aid for Scientific Research from Ministry of Education, Science and Culture, Japan.

References and Notes

1 J.-M.Lehn, *Angw.Chem., Int.Ed.Engl.*, **29**, 1304 (1990).
2 J.Yang, E.Fan, S.J.Geib, A.Hamilton, *J.Am.Chem.Soc.*, **115**, 5314 (1993).
3 J.P.Mathias, C.T.Seto, E.E.Simanek, G.M.Whitesides, *J.Am.Chem.Soc.*, **116**, 1725 (1994).
4 F.Ciuchi, G.D.Nicola, H.Franz, G.Gottrarelli, P.Mariani, M.G.P.Bossi, G.P.Spada, *J.Am.Chem.Soc.*, **116**, 7064 (1994).
5 H.Ringsdorf, B.Schlarb, J.Venzmer, *Angw.Chem., Int.Ed.Engl.*, **27**, 113 (1988).
6 Y.Kang, K.Araki, K.Iwamoto, M.Seno, *J.Appl.Polym.Sci.*, **27**, 2025 (1982).
7 K.K.Ogilvie, A.L.Schifman, C.L.Penney, *Can.J.Chem.*, **57**, 2230 (1979).
8 Measurement was performed on a Max Science MXC18 with Cu-α radiation, and structure was determined from 2018 unique reflections, refinement with a SHELXS program. Crystal Data: C31H67N5O8Si3, Mw=722, crystal size 0.5x0.5x0.8 mm^3, orthorhombic, space group B2212(# 20), unit cell a=19.369, b=33.473, and c=12.879 Å, unit cell volume 8350 Å^3, Z=8, R=0.071, Rw=0.066, unique reflections 3834.
9 Role of methanol is comparable to that of alcohol in lyotropic mesophase of surfactant-water-alcohol systems, in which alcohol serves as a co-surfactant tuning electrostatic interaction between head groups of the surfactant.