Effect of a Polymethylene Chain on the Intramolecular Hydrogen Bond between Adenine and Thymine

Toshio Itahara

Department of Bioengineering, Faculty of Engineering, Kagoshima University, Korimoto, Kagoshima 890-0065

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The intramolecular hydrogen bond between the adenine and thymine rings of 9-[ω-(thymin-1-yl)alkyl]adenine was investigated in chloroform by means of NMR spectroscopy. The formation of the intramolecular hydrogen bond was dependent on the length of the polymethylene chains between adenine and thymine, and the thermodynamic parameters were estimated. The length of the polymethylene chains caused a marked difference in the physical properties of the compounds.

A molecular assembly formed by hydrogen bonds has been paid attention concerning applications as a material, such as a liquid crystal.[1] Nucleic base pairing is a well-known example of the hydrogen bond. The formation of a hydrogen bond between adenine and thymine has been extensively investigated by several groups of workers.[2–5] In a classical study by nuclear magnetic resonance (NMR) spectroscopy,[2] it became known that the chemical shifts of the NH of thymine ring (Thy-NH) and of the NH_2 of the adenine ring (Ade-NH_2) are to lower fields when the hydrogen bond is formed. Recent investigations appear to be directed toward the hydrogen bond between adenine and thymine (or uracil) connected with some linkers.[3,4] The literature contains several references to the intramolecular hydrogen bond between adenine and thymine.[3] However, little attention has been paid to the relationship between the intramolecular hydrogen bond and the length of the linkers, although the effect of the length of the linkers on the intramolecular hydrogen bond between two thymine rings was reported.[5] In order to study the relationship, 9-[ω-(thymin-1-yl)alkyl]adenines (**1a–g**, Chart 1) (n = 12–6) were prepared. The relationship of **1a–g** was investigated in chloroform by NMR spectroscopy. Furthermore, the characteristics of **1** were studied by means of infrared (IR) spectroscopy, differential scanning calorimetry (DSC), and polarizing microscopy.

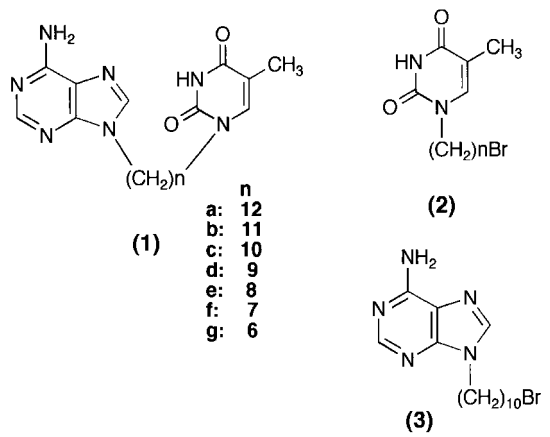

Chart 1.

Results and Discussion

While the alkylation of thymine in the presence of a base is generally known to give 1,3-dialkylthymine, we previously reported on the preparation of 1-(ω-bromoalkyl)thymine (**2c–g**) by a treatment of thymine with $Br(CH_2)_nBr$ (n = 10–6) in the presence of ^{t}BuOK.[6] A similar treatment of thymine with $Br(CH_2)_{12}Br$ and $Br(CH_2)_{11}Br$ gave **2a**[7] and **2b**, respectively. Reaction of adenine and **2a–g** gave 9-[ω-(thymin-1-yl)alkyl]adenine (**1a–g**) (n = 12–6), although the synthesis of 9-[3-(thymin-1-yl)propyl]adenine (**1**) (n = 3) had already been reported.[8]

The concentration dependence on the ^{1}H NMR chemical shifts of **1a**, **1b**, and **1c** (n = 12, 11, and 10) in $CDCl_3$ was studied (Fig. 1). The chemical shifts of Thy-NH and Ade-NH_2

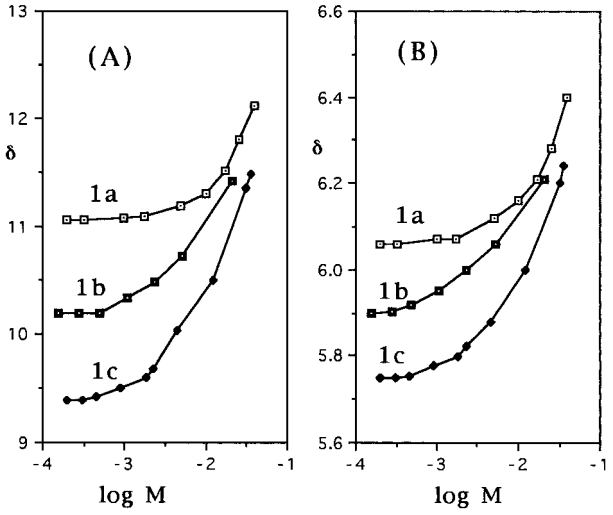

Fig. 1. Concentration dependence on the chemical shifts of (**A**) the NH of thymine ring and (**B**) the NH_2 of adenine ring of **1a**, **1b**, and **1c**, in $CDCl_3$ at 27 °C.

Table 1. ^{1}H-NMR Chemical Shifts of **1** in $CDCl_3$ at 27 °C[a)]

1	*n*	Ade-2	Ade-8	Ade-NH_2	Thy-6	Thy-Me	Thy-NH
1a	12	8.37	7.99	6.06	6.96	1.93	11.07
1b	11	8.37	7.94	5.90	6.96	1.93	10.19
1c	10	8.37	7.88	5.75	6.96	1.92	9.38
1d	9	8.37	7.82	5.66	6.95	1.92	8.54
1e	8	8.37	7.81	5.59	6.95	1.92	8.15
1f	7	8.37	7.80	5.59	6.94	1.92	8.15
1g	6	8.37	7.80	5.59	6.94	1.91	8.17

a) The concentrations in $CDCl_3$ were less than 0.25 mM.

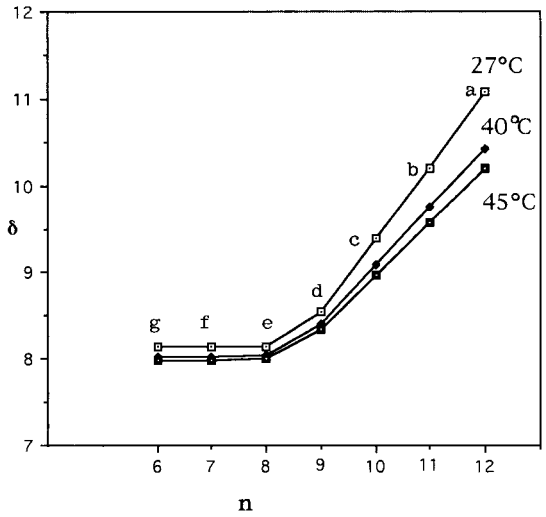

Fig. 2. Relationship between the chemical shifts of the NH of thymine ring of **1a–g** (less than 0.25 mM) and the carbon number of the polymethylene chains.

were to lower fields along with an increase in the concentrations. The down-field shifts of the chemical shifts were attributable to the formation of an intermolecular hydrogen bond.[2] However, the ^{1}H NMR chemical shifts of **1a–g** (n = 12–6) were hardly shifted in lower concentrations than 0.25 mM. The ^{1}H NMR chemical shifts of **1a–g** at 27 °C are summarized in Table 1. The relationship between the chemical shifts of Thy–NH (Table 1) and the carbon numbers of the polymethylene chains is shown in Fig. 2. The chemical shifts of Thy–NH of **1a–d** (n = 12–9) were to lower fields along with an increase in the length of the polymethylene chain, compared with the chemical shifts of **1e–g** (n = 8–6). The results can be interpreted as involving the formation of an intramolecular hydrogen bond between the adenine and the thymine rings of **1a–d**, although a similar interpretation has already been reported.[3] On the other hand, the chemical shift of **1e** was very similar to those of **1f** and **1g**. This suggests that the adenine and the thymine rings of **1e–g** did not form an intramolecular hydrogen bond because of the shortness of the polymethylene chains.

From the standpoint of the formation of a hydrogen bond, the association between the adenine and the thymine of **1** exists in three forms (Chart 2): an open form (no hydrogen bond), a closed form (intramolecular hydrogen bond), and an aggregated form (intermolecular hydrogen bond). The chemical shift of Thy-NH of **1e–g**, shown in Fig. 2, corresponded to that of open form, because not only the closed form, but also the aggregated form, were negligible when the measurement was carried out at lower concentrations than 0.25 mM. Taking account of the results that the chemical shifts of Thy-NH involving the open form of **1e–g** were similar to each other, it is also expected that hardly even the chemical shifts of Thy-NH of the open form of **1a–d** were influenced by the length of the polymethylene chains. Therefore, the chemical shifts (δ_{open}) of the open form of **1a–d** were presumed to be δ 8.15 (27 °C), δ 8.02 (40 °C), and δ 7.98 (45 °C). On the other hand, the observed chemical shifts ($\delta_{observed}$) of **1a–c** are thought to originate from the equilibrium between the open form and the closed form at 27 °C, 40 °C, and 45 °C. That is, the observed down-field shifts of **1a–d** (Fig. 2) can be regarded as an increase of the closed form.

To determine the chemical shift of the closed form, the titration of **1a–c** with 9-(10-bromodecyl)adenine (**3**)[9] was studied. Figure 3A shows titration curves of Thy-NH of **1a** at 27 °C, 40 °C, and 45 °C. When a large excess amount of **3** was added

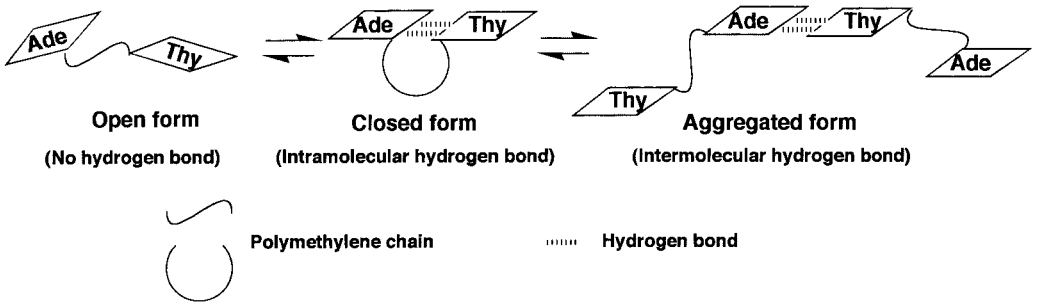

Chart 2.

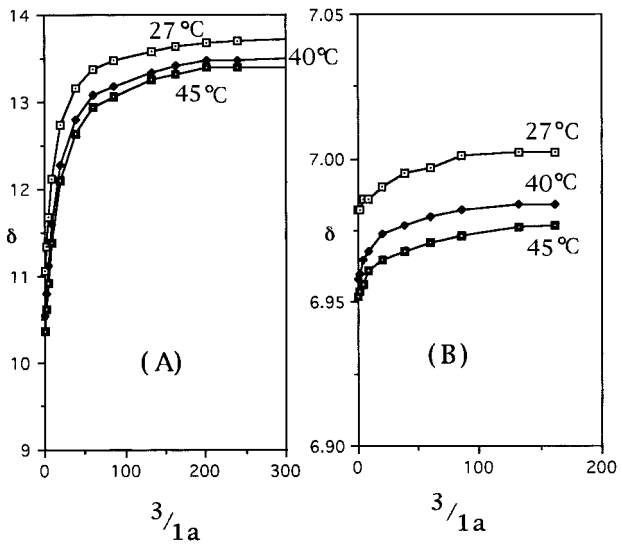

Fig. 3. Titration curves of **1a** with **3** in $CDCl_3$ at 27 °C, 40 °C, and 45 °C: (**A**) the chemical shift of the NH of thymine ring and (**B**) the chemical shifts of the H-6 of thymine ring vs the ratio of **3** (mmol) to **1a** a (1.5 mmol).

Table 2. The Values of the Chemical Shift of Thy-NH for the Thermodynamic Parameters

	Temp/°C	δ_{open} [a)]	δ_{closed} [b)]	$\delta_{observed}$ [a)]
1a	27	8.15	13.71	11.07
	40	8.02	13.50	10.42
	45	7.98	13.41	10.20
1b	27	8.15	13.73	10.19
	40	8.02	13.54	9.76
	45	7.98	13.44	9.58
1c	27	8.15	13.73	9.38
	40	8.02	13.52	9.08
	45	7.98	13.42	8.97

a) The values of δ_{open} and $\delta_{observed}$ were obtained from Fig. 2. b) The values of δ_{closed} were obtained from the titration curves with **3** (Fig. 3A).

into a solution containing **1a–c**, the chemical shifts of **1a** were similar to those of **1b** and **1c**. Although the chemical shifts are expected to be those of the closed form of **1a–c**, adding a large amount of **3** may cause an increase in the stacked conformers between **1** and **3**. To determine the effect on the stacking, the titration curves of the proton at the 6-position (Thy-6) and the methyl group (Thy-Me) of thymine ring of **1a–c** were compared with those of Thy-NH (Fig, 3A). Figure 3B shows titration curves of the proton at the 6-position of the thymine ring (Thy-6) of **1a**. The chemical shifts of both Thy-6 and Thy-Me were not shifted to higher fields along with an increase in the concentrations of **3**. Therefore, the stacking may be substantially negligible in $CDCl_3$. Based on the titration (Fig. 3A), the chemical shifts (δ_{closed}) of the closed form of **1a–c** were determined (Table 2).

The equilibrium constants (K = [closed form]/[open form]) were calculated as follows:

$$K = (\delta_{observed} - \delta_{open})/(\delta_{closed} - \delta_{observed}).$$

The enthalpy and entropy change values of the intramolecular hydrogen bond between the adenine and the thymine rings of **1a–c** were determined by plotting logK against ($1/T$) using

$$\log K = (-\Delta H/2.3R)(1/T) + (\Delta S/2.3R).$$

The thermodynamic parameters were as follows: **1a**: $\Delta H = -21 \pm 2$ KJ mol^{-1}, $\Delta S = -69 \pm 7$ J K^{-1} mol^{-1}; **1b**: $\Delta H = -15 \pm 2$ KJ mol^{-1}, $\Delta S = -54 \pm 6$ J K^{-1} mol^{-1}; **1c**: $\Delta H = -11 \pm 2$ KJ mol^{-1}, $\Delta S = -47 \pm 5$ J K^{-1} mol^{-1}. The values of ΔH determined in the present experiments were smaller compared with the value reported for the intermolecular hydrogen bond ($\Delta H = -26 \pm 2$ KJ mol^{-1}).[10] Also, the values were decreased along with a decrease in the length of the polymethylene chains. These results may be interpreted as a bond-length and/or bond-angle strain at the site of the intramolecular hydrogen bond.[3a]

From a consideration of the above results, the molecular assembly of **1a** is expected to be something different from that of **1e–g**. In addition to the IR spectral data of **1a–e** in $CDCl_3$, shown in Experimental part, the IR spectroscopy of the solid state of **1a**, **1c**, **1e**, and **1f** was further studied. The IR spectra of **1a**, **1c**, and **1f** in the range of 3000 to 3600 cm^{-1} are shown in Fig. 4. From a comparison of the spectra in the solution (Experimental) and the results that had already been reported,[10] it is conceivable that those bands originated from the hydrogen bond. The bands of **1e** and **1f** were broad compared with those of **1a** and **1c**. Furthermore, compounds **1** displayed major peaks at lower wave numbers as the length of the polymethylene chain became short. It is estimated that the characteristic bands of **1a** originated from an intramolecular hydrogen bond, but the broad bands of **1f** were generated from an intermolecular hydrogen bond. The intermolecular interaction of **1e–g** may further lead to the formation of polymeric structures, which are paid attention as liquid crystal.[1,11]

In order to examine the liquid crystalline properties of **1**, differential scanning calorimetry (DSC) and polarizing microscopy of **1a** and **1e** were studied. Although neither **1a** nor **1e** exhibited any thermotropic liquid crystalline property, the DSC thermogram of **1a** was different from that of **1e** (Fig. 5). As can be seem from Fig. 5, **1e** did not crystallize upon cool-

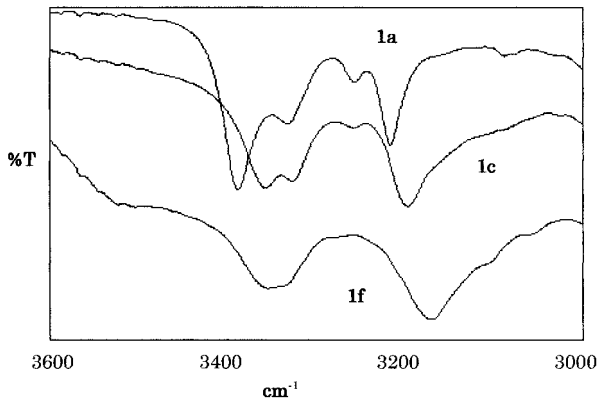

Fig. 4. Infrared spectra of the solid states of **1a**, **1c**, and **1f**. **1a**: 3388, 3333, 3257 3217 cm^{-1}. **1c**: 3358, 3328, 3258, 3197 cm^{-1}. **1f**: 3355, 3170 cm^{-1}.

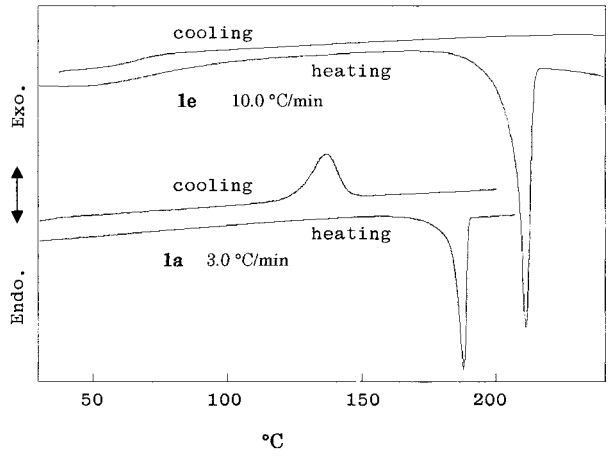

Fig. 5. DSC thermograms of **1a** and **1e**.

ing, and made a glass state at room temperature. On the other hand, a polarizing microscopy observation of **1a** showed its characteristic optical texture, which depended on the cooling process. Compound **1a** crystallized spontaneously upon slowly cooling to give birefringent solids. The optical texture is shown in Fig. 6A. On the other hand, when we cooled **1a** rapidly to room temperature, **1a** showed a different optical texture (Fig. 6B). Also, the fast atom bombardment (FAB) mass spectra of **1a–c** showed peaks of not only $(M+1)^+$, but also $(2M+1)^+$ (Experimental). Further work is in progress on the structure of the solid of **1a.**

Experimental

General. The melting points were determined on a Yanagimoto micro melting-point apparatus and are uncorrected. The elemental analyses were performed by the Analytical Center of Kyoto University. The ^{1}H NMR spectra (400 MHz) and ^{13}C NMR spectra (100 MHz) were obtained with a JEOL GSX400 spectrometer. The chemical shifts (δ-values) were measured in parts per million (ppm) down-field from tetramethylsilane as an internal reference. The ^{1}H NMR spectra were obtained from the accumulation of 40–2200 free induction decays after each 45° pulse (5.7 μs) repeated every 5.73 s, and were observed over a spectral width of 6002.4 Hz, corresponding to 32768 data points for an acquisition time of 2.73 s. Some of the ^{1}H NMR spectra in $CDCl_3$, such as the titrations, were observed over a spectral width of 9009.0 Hz. The infared spectra were recorded on a JASCO FT/IR-420 spectrometer and the measurements in $CDCl_3$ were made at room temperature with a 0.1-mm KBr cell. The IR spectra of the solids were measured with disposable IR cards (3M Type 61, USA). After the sample solution in chloroform was added to the IR card, the card was dried at room temperature. FAB mass spectra were recorded with a JEOL JMS-SX 102A spectrometer. Differential scanning calorimetry (DSC) measurements were carried out with a Shimadzu DSC-60. Optical microscopy observations were performed by employing a Nikon Eclipse E600 POL polarizing microscope equipped with a hot stage (Tokai Hit ThermoPlate).

Alkylation of Thymine. Into a solution of thymine (10 mmol) in DMF (150 mL), ^{t}BuOK (5 mmol) and $Br(CH_2)_nBr$ (n = 11 or 12) (10 mmol) were added. The mixture was stirred at room temperature for 15 h. The resulting mixture was evaporated to give a residue which was submitted to chromatography over silica gel. By the elution of ethyl acetate, 1-(ω-bromoalkyl)thymine (**2a**) (n = 12:21%) or (**2b**) (n = 11:15%) was obtained. The preparation of **2c–g** (n = 10–6) was already reported.[6]

1-(12-Bromododecyl)thymine (2a): Mp 102–103 °C (lit.[7] 104–106 °C); ^{1}H NMR ($CDCl_3$) δ 9.06 (s, 1H, NH), 6.98 (q, 1H, J = 1 Hz), 3.69 (t, 2H, J = 7 Hz), 3.41 (t, 2H, J = 7 Hz), 1.92 (d, 3H, J = 1 Hz), 1.85 (quintet, 2H, J = 7.2 Hz), 1.67 (broad quintet, 2H, J = 7 Hz), 1.42 (broad quintet, 2H, J = 7 Hz), 1.35–1.25 (broad, 14H); ^{13}C NMR ($CDCl_3$) δ 164.30, 150.89, 140.41, 110.52, 48.57, 34.04, 32.83, 29.45, 29.44, 29.41, 29.38, 29.18, 29.10, 28.74, 28.15, 26.43, 12.33.

1-(11-Bromoundecyl)thymine (2b): Mp 97–98 °C; ^{1}H NMR ($CDCl_3$) δ 8.63 (s, 1H, NH), 6.97 (q, 1H, J = 1 Hz), 3.68 (t, 2H, J = 7.2 Hz), 3.41 (t, 2H, J = 7 Hz), 1.93 (d, 3H, J = 1 Hz), 1.85 (quintet, 2H, J = 7 Hz), 1.67 (broad quintet, 2H, J = 7 Hz), 1.42 (broad quintet, 2H, J = 7 Hz), 1.35–1.25 (broad, 12H); ^{13}C NMR ($CDCl_3$) δ 164.07, 150.75, 140.39, 110.52, 48.57, 34.04, 32.81, 29.38, 29.38, 29.36, 29.16, 29.11, 28.72, 28.15, 26.43, 12.33. Found: C, 53.48; H, 7.68; N, 7.61%. Calcd for $C_{16}H_{27}N_2O_2Br$: C, 53.49; H, 7.57; N, 7.80%.

9-[ω-(Thymin-1-yl)alkyl]adenine (1). Into a solution of adenine (1 mmol) in DMF (30 mL), 1-(ω-bromoalkyl)thymine (**2a–g**) (n = 12–5) (1 mmol) and K_2CO_3 (1 mmol) were added. The mixture was stirred at room temperature for 15 h. The resulting mix-

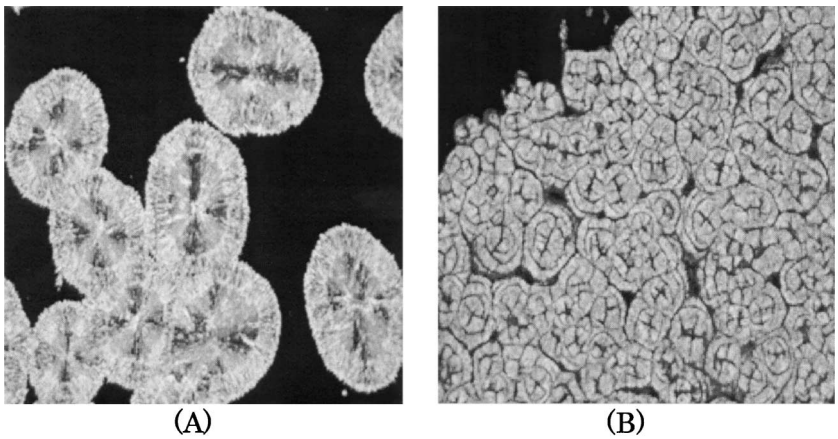

Fig. 6. Optical textures obtained by polarizing microscopy of **1a** (the solid state) at room temperature upon cooling from the melt. (**A**) Cooling slowly (magnification 100 ×). (**B**) Cooling rapidly (magnification 200 ×).

ture was evaporated to give a residue which was submitted to chromatography over silica gel. By elution of a mixture of ethyl acetate and methanol, 9-[ω-(thymin-1-yl)alkyl]adenine (**1**) [**1a**: 34%; **1b**: 30%; **1c**: 35%; **1d**: 28%; **1e**: 28%; **1f**: 22%; **1g**: 22%] was obtained.

9-[12-(Thymin-1-yl)dodecyl]adenine (1a): Mp 188–190 °C; ^{1}H NMR ($CDCl_3$) δ 11.88 (s, 1H), 8.39 (s, 1H), 7.99 (s, 1H), 6.99 (s, 1H), 6.31 (broad s, 2H), 4.21 (t, 2H, J = 7 Hz), 3.73 (t, 2H, J = 7 Hz), 1.94 (s, 3H), 1.91 (quintet, 2H, J = 7 Hz), 1.69 (quintet, 2H, J = 7 Hz), 1.4–1.2 (broad, 16H); ^{1}H NMR (DMSO-d_6) δ 11.19 (s, 1H, T-NH), 8.13 (s, 1H, A-2 or 8), 8.12 (s, 1H, A-2 or 8), 7.52 (s, 1H, T-6), 7.16 (s, 2H, NH_2), 4.12 (t, 2H, J = 7 Hz), 3.59 (t, 2H, J = 7 Hz), 1.79 (quintet, 2H, J = 7 Hz), 1.74 (s, 3H), 1.54 (broad quintet, 2H, J = 7 Hz), 1.20 (broad, 16H); ^{13}C NMR ($CDCl_3$) δ 165.31, 155.63, 153.14, 151.53, 150.05, 140.76, 140.33, 119.05, 110.59, 47.76, 43.78, 29.61, 29.22, 29.18, 29.14, 29.07, 29.02, 28.69, 26.25, 26.01, 12.37. IR ($CDCl_3$) 3528 (free NH_2), 3482 (hydrogen bond), 3404 (free NH_2 and free Thy-NH), 3333 (hydrogen bond), 3258 (hydrogen bond), 3207 (hydrogen bond), 1698, 1685, 1642 cm^{-1}. FABMS, m/z 855 (2M+1), 720, 428 (M+1, 100%). HRFABMS m/z Calcd for $C_{22}H_{34}N_7O_2$ (M+1) 428.2774, found 428.2775. Found: C, 62.07; H, 7.82; N, 22.63%. Calcd for $C_{22}H_{33}N_7O_2$: C, 61.80; H, 7.78; N, 22.93%.

9-[11-(Thymin-1-yl)undecyl]adenine (1b): Mp 178–180 °C; ^{1}H NMR ($CDCl_3$) δ 11.41 (s, 1H), 8.39 (s, 1H), 7.96 (s, 1H), 6.98 (s, 1H), 6.26 (broad s, 2H), 4.21 (t, 2H, J = 7 Hz), 3.71 (t, 2H, J = 7 Hz), 1.93 (s, 3H), 1.87 (quintet, 2H, J = 7 Hz), 1.67 (quintet, 2H, J = 7 Hz), 1.35–1.2 (broad, 14H); ^{13}C NMR ($CDCl_3$) δ 165.16, 155.64, 153.12, 151.50, 150.05, 140.72, 140.44, 119.11, 110.60, 48.21, 43.90, 29.88, 29.28, 29.27, 29.27, 28.92, 28.85, 28.79, 26.34, 26.12, 12.36. IR ($CDCl_3$) 3525, 3483, 3406, 3332, 3257, 3207, 1698, 1685, 1640 cm^{-1}. FABMS, m/z 827 (2M+1), 692, 414 (M+1, 100%). HRFABMS m/z Calcd for $C_{21}H_{32}N_7O_2$ (M+1) 414.2617, found 414.2622. Found: C, 60.58; H, 7.55; N, 23.51%. Calcd for $C_{21}H_{31}N_7O_2\cdot 1/4H_2O$: C, 60.33; H, 7.59; N, 23.45%.

9-[10-(Thymin-1-yl)decyl]adenine (1c): Mp 186–188 °C; ^{1}H NMR ($CDCl_3$) δ 11.66 (s, 1H), 8.40 (s, 1H), 7.96 (s, 1H), 6.98 (s, 1H), 6.32 (broad s, 2H), 4.20 (t, 2H, J = 7 Hz), 3.70 (t, 2H, J = 7 Hz), 1.94 (s, 3H), 1.91 (quintet, 2H, J = 7 Hz), 1.70 (quintet, 2H, J = 7 Hz), 1.35–1.2 (broad, 12H); ^{13}C NMR ($CDCl_3$) δ 165.20, 155.66, 153.08, 151.51, 150.08, 140.61, 140.41, 119.12, 110.61, 48.27, 43.95, 29.86, 29.11, 29.09, 29.08, 28.91, 28.80, 26.41, 26.22, 12.36. IR ($CDCl_3$) 3524, 3484, 3407, 3332, 3258, 3207, 1699, 1685, 1638 cm^{-1}. FABMS, m/z 799 (2M+1), 664, 400 (M+1, 100%). HRFABMS m/z Calcd for $C_{20}H_{30}N_7O_2$ (M+1) 400.2461, found 400.2462. Found: C, 60.30; H, 7.29; N, 24.27%. Calcd for $C_{20}H_{29}N_7O_2$: C, 60.13; H, 7.32; N, 24.54%.

9-[9-(Thymin-1-yl)nonyl]adenine (1d): Mp 190–192 °C; ^{1}H NMR ($CDCl_3$) δ 11.36 (s, 1H), 8.40 (s, 1H), 7.93 (s, 1H), 6.98 (s, 1H), 6.33 (broad s, 2H), 4.20 (t, 2H, J = 7 Hz), 3.68 (t, 2H, J = 7 Hz), 1.93 (s, 3H), 1.91 (quintet, 2H, J = 7 Hz), 1.66 (quintet, 2H, J = 7 Hz), 1.35–1.2 (broad, 10H); ^{13}C NMR ($CDCl_3$) δ 165.07, 155.68, 153.08, 151.48, 150.05, 140.59, 140.36, 119.16, 110.65, 48.35, 43.94, 29.89, 29.03, 29.01, 28.79, 28.74, 26.39, 26.24, 12.36. IR ($CDCl_3$) 3524, 3484, 3405, 3332, 3259, 3206, 1699, 1685, 1633 cm^{-1}. Found: C, 58.59; H, 7.23; N, 25.26%. Calcd for $C_{19}H_{27}N_7O_2\cdot 1/3H_2O$: C, 58.30; H, 7.12; N, 25.05%.

9-[8-(Thymin-1-yl)octyl]adenine (1e): Mp 216–218 °C; ^{1}H NMR ($CDCl_3$) δ 10.35 (s, 1H), 8.39 (s, 1H), 7.89 (s, 1H), 6.97 (s, 1H), 5.98 (broad s, 2H), 4.20 (t, 2H, J = 7 Hz), 3.68 (t, 2H, J = 7 Hz), 1.93 (s, 3H), 1.90 (quintet, 2H, J = 7 Hz), 1.66 (quintet, 2H, J = 7 Hz), 1.35–1.2 (broad, 8H); ^{13}C NMR ($CDCl_3$) δ 164.61, 155.52, 153.08, 151.09, 150.13, 140.63, 140.34, 119.39, 110.62, 48.32, 43.92, 29.92, 29.06, 28.83, 28.77, 26.42, 26.16, 12.35. IR ($CDCl_3$) 3524, 3486, 3409, 3257, 1699, 1684, 1631 cm^{-1}. FABMS, m/z 372 (M+1, 100%). HRFABMS m/z Calcd for $C_{18}H_{26}N_7O_2$ (M+1) 372.2148, found 372.2145. Found: C, 57.24; H, 6.74; N, 25.72%. Calcd for $C_{18}H_{25}N_7O_2\cdot 1/3H_2O$: C, 57.27; H, 6.85; N, 25.98%.

9-[7-(Thymin-1-yl)heptyl]adenine (1f): Mp 197–200 °C; ^{1}H NMR (DMSO-d_6) δ 11.18 (s, 1H, T-NH), 8.14 (s, 1H, A-2 or 8), 8.13 (s, 1H, A-2 or 8), 7.50 (s, 1H, T-6), 7.15 (s, 2H, NH_2), 4.12 (t, 2H, J = 7 Hz), 3.59 (t, 2H, J = 7 Hz), 1.79 (quintet, 2H, J = 7 Hz), 1.74 (s, 3H), 1.53 (broad quintet, 2H, J = 7 Hz), 1.29 (broad quintet, 2H, J = 7 Hz), 1.22 (broad quintet, 4H, J = 7 Hz); ^{13}C NMR (DMSO-d_6) δ 164.20, 155.83, 152.23, 150.77, 149.45, 141.33, 140.74, 118.61, 108.29, 46.96, 42.72, 29.17, 28.24, 27.91, 25.78, 25.66, 11.81. Found: C, 57.25; H, 6.66; N, 27.67%. Calcd for $C_{17}H_{23}N_7O_2$: C, 57.13; H, 6.49; N, 27.43%.

9-[6-(Thymin-1-yl)hexyl]adenine (1g): Mp 220–224 °C; ^{1}H NMR (DMSO-d_6) δ 11.20 (s, 1H, T-NH), 8.14 (s, 1H, A-2 or 8), 8.13 (s, 1H, A-2 or 8), 7.51 (s, 1H, T-6), 7.17 (s, 2H, NH_2), 4.12 (t, 2H, J = 7 Hz), 3.59 (t, 2H, J = 7 Hz), 1.80 (quintet, 2H, J = 7 Hz), 1.74 (s, 3H), 1.54 (broad quintet, 2H, J = 7 Hz), 1.26 (broad, 4H); ^{13}C NMR (DMSO-d_6) δ 164.19, 155.83, 152.23, 150.78, 149.47, 141.30, 140.71, 118.65, 108.30, 46.88, 42.65, 29.11, 28.51, 25.51, 25.16, 11.79. Found: C, 56.12; H, 6.13; N, 28.83%. Calcd for $C_{16}H_{21}N_7O_2$: C, 55.96; H, 6.16; N, 28.55%.

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