Polymer Vol. 37 No. 4, pp. 667–673, 1996

0032-3861/96/$15.00 + 0.00

Synthesis and physico-chemical properties of alternating copolymers of maleic anhydride with dihydropyrans containing 6-chloropurine, 6-mercaptopurine, and hypoxanthine*

Man Jung Han†, Sang Wook Park, Tae Joon Cho and Ji Young Chang
Department of Applied Chemistry, Ajou University, Suwon 441-749, Republic of Korea

The new monomers, 2-(6-chloro-, 6-hydroxy-, 6-mercapto-, and 6-aminopurin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3a**, **3b**, **3c**, and **3d**, respectively) and 2-(6-chloro and 6-hydroxypurin-7-ylmethyl)-3,4-dihydro-2*H*-pyran (**4a** and **4b**, respectively) were synthesized. Copolymerization of these monomers with maleic anhydride resulted in the alternating copolymers **5** and **7**, which were hydrolysed to give poly[(2-(6-Cl-, OH-, and SH-purin-9-ylmethyl)tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)])(6a, **6b**, and **6c**, respectively) and poly[(2-(6-Cl- and OH-purin-7-ylmethyl) tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)] (**8a** and **8b**, respectively). The polymers **6** and **8** are polynucleotide analogues, which have 6-chloropurine, hypoxanthine or 6-mercaptopurine as nucleic acid bases. They showed physico-chemical properties quite similar to those of the natural polynucleotides, e.g. polymer **6b** showed 23.7% of hypochromicity of the u.v. absorption at a wavelength of 250 nm, and **8b** exhibited a broad excimer fluorescence around 422 nm and showed typical polyelectrolyte behaviour.

(Keywords: polynucleotide analogue; hypochromicity; polyelectrolyte)

INTRODUCTION

Many attempts have been made to synthesize polynucleotide analogues (PNAs) as model compounds for natural polymers in an effort to elucidate the functions of nucleic acids in biological systems and utilize their biological activities in the design of polymeric drugs for chemotherapy. PNAs have been synthesized by several methods; namely polymerization of vinyl monomers containing nucleic acid bases (NABs)[1–6], grafting of NABs on to selected polymer chains[7–18], and polycondensations of ω-hydroxy carboxylic acids or α-amino acids which contain NABs[19–21]. Compared with the natural polynucleotides, the synthesized PNAs showed several drawbacks: most of the reported PNAs exhibited neither good solubilities in water, due to their lack of hydrophilic groups, nor good optical activities, due to the absence of sugar moieties on the polymer chain. The alternating sequences between nucleosides and phosphate, observed in natural polynucleotides, were rarely realized in synthetic PNAs.

In our previous papers[22–26], we have reported the synthesis of several PNAs in which either the methylene phosphate groups of natural polynucleotides were substituted by dicarboxyethylene groups or the furanose sugar moieties were replaced by pyranose rings. These PNAs were soluble in water, resistant to hydrolysis, and optically active. They contained alternating sequences between nucleoside analogues and dicarboxyethylene groups along the polymer chains. They have also shown physico-chemical properties quite similar to those of the natural polymers, such as hypochromicity and polyelectrolyte behaviours. In line with an effort to obtain PNAs closely resembling the natural polymers and to study their physico-chemical properties, we have synthesized five new PNAs containing purine bases, as shown in *Scheme 2*. We report here their synthesis and physico-chemical properties.

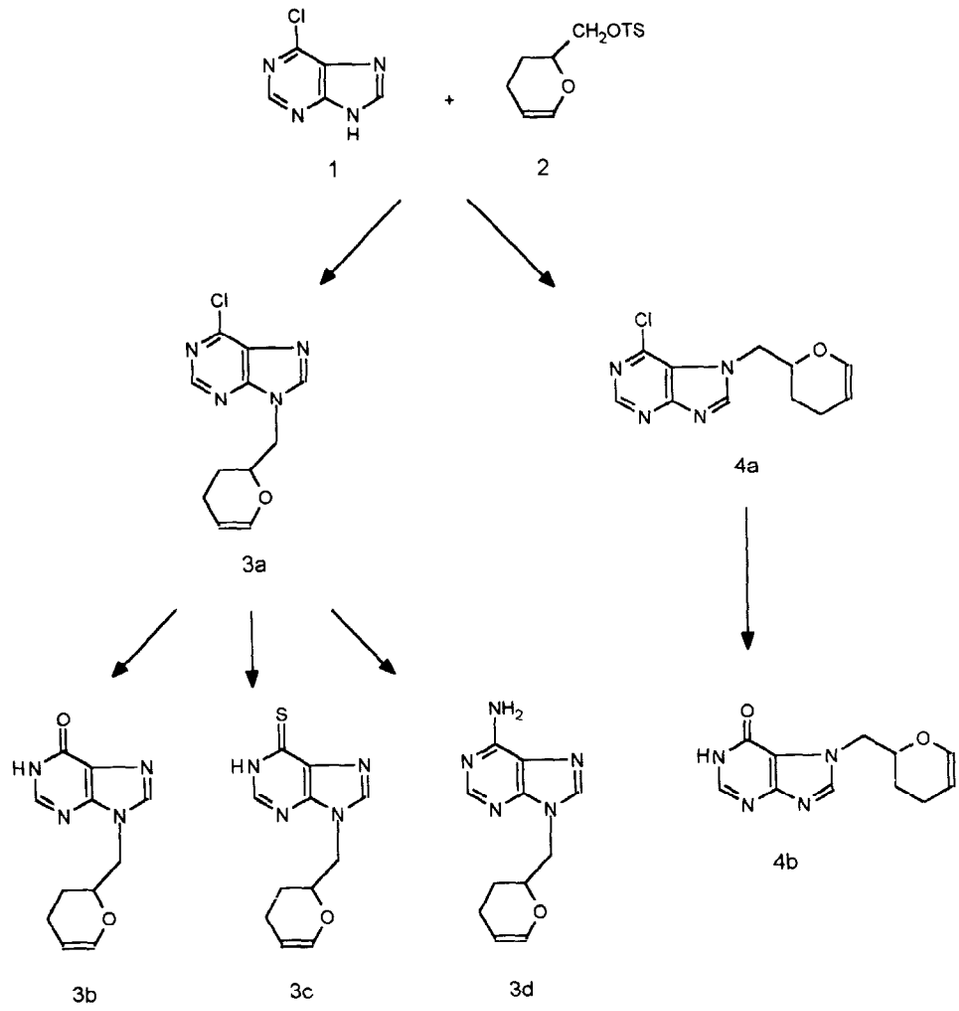
EXPERIMENTAL

Materials

6-Chloropurine (Aldrich, 99%), NaH, and 40% aqueous trimethylamine solution were used as received. Maleic anhydride and azoisobutyronitrile (AIBN) were recrystallized from benzene and methanol, respectively. Acetic anhydride and pyridine were distilled before use. *N*, *N*-Dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were dried over anhydrous $MgSO_4$ and then distilled. Other commercially available reagent chemicals were used without purification.

2-Formyl-3,4-dihydro-2*H*-pyran was synthesized by the Diels–Alder reaction of acrolein[27]. 2-(Tosyloxymethyl)-3,4-dihydro-2*H*-pyran (**2**) was prepared by the reaction of

* Paper no. 8 in a series on polynucleotide analogues
† To whom correspondence should be addressed



Scheme 1

tosyl chloride with 2-(hydroxymethyl)-3,4-dihydro-2*H*-pyran[28], which was synthesized by the reduction of 2-formyl-3,4-dihydro-2*H*-pyran with the aid of $NaBH_4$.

Synthesis of monomers

*2-(6-Chloropurin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3a**) and 2-(6-chloropurin-7-ylmethyl)-3,4-dihydro-2*H*-pyran (**4a**).* 6-Chloropurine (1 g, 6.47 mmol) and potassium carbonate (1.07 g, 7.76 mmol) were dissolved in 80 ml of DMSO and stirred for 30 min at room temperature. After adding 2.66 g (9.7 mmol) of 2-tosyloxymethyl-3,4-dihydro-2*H*-pyran, the solution was stirred for 12 h at 70°C. The syrupy compounds **3a** and **4a** were separated by column chromatography on silica gel (CCl_4: acetone = 7:3 vol/vol). Compound **3a** solidified in hexane to give 1.46 g of product (m.p. 126–128°C, yield 39.9%) and **4a** crystallized in ethyl acetate to give 0.17 g of product (m.p. 102–103°C, yield 4.5%).

^{1}H n.m.r., **3a** (200 MHz, DMSO-d_6), δ (ppm): for 2-methylhydropyran 1.43–1.65 (m, 1H, H_{3a}), 1.9–2.4 (m, 3H, H_{3b}, H_4), 4.1–4.25 (m, 1H, H_2), 4.3–4.64 (m, 2H, H_{10}), 4.68–4.8 (m, 1H, H_5), 6.32, 6.35 (d, 1H, J = 6 Hz, H_6); for chloropurine 8.24 (s, 1H, H_8), 8.75 (s, 1H, H_2). ^{1}H n.m.r., **4a** (200 MHz, DMSO-d_6, δ (ppm): for 2-methylhydropyran 1.5–1.84 (m, 1H, H_{3a}), 1.95–2.4 (m, 3H, H_{3b}, H_4), 4.1–4.25 (m, 1H, H_2), 4.45–4.62 (m, 2H, H_{10}), 4.68–4.84 (m, 1H, H_5), 6.31, 6.28 (d, 1H, J = 6 Hz, H_6); for 6-chloropurine 8.3 (s, 1H, H_8), 8.89 (s, 1H, H_2). Elemental analysis, calcd for $C_{11}H_{11}N_4OCl$: C, 52.7; H, 4.4; N, 22.4%. Found: C, 52.4; H, 4.46; N, 21.7%.

*2-(Hypoxanthin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3b**) and 2-(hypoxanthin-7-ylmethyl)-3,4-dihydro-2*H*-pyran (**4b**).* Compound **3a** (0.6 g, 2.4 mmol) or **4a** (0.1 g, 0.4 mmol) was dissolved in 70 ml of 30% trimethylamine and stirred for 5 h at room temperature. After evaporating the solvent, the residues were crystallized in ethanol to give 0.31 g of **3b** (m.p. 129–132°C, yield 52%) or 0.0435 g of **4b** (m.p. 218°C (dec.), yield 43.5%).

^{1}H n.m.r., **3b** (200 MHz, DMSO-d_6), δ (ppm): for 2-methylhydropyran 1.35–1.58 (m, 1H, H_{3a}), 1.8–2.18 (m, 3H, H_{3b}, H_4), 4.1–4.25 (m, 1H, H_2), 4.25–4.4 (m, 2H, H_{10}), 4.62–4.75 (m, 1H, H_5), 6.33, 6.36 (d, 1H, H, J = 6 Hz, H_6); for hypoxanthine 8.04 (s, 2H, H_2, H_8), 12.32 (bs, 1H, NH). ^{1}H n.m.r., **4b** (200 MHz, DMSO-d_6), δ (ppm): for 2-methylhydropyran 1.3–1.6 (m, 1H, H_{3a}), 1.62–2.1 (m, 3H, H_{3b}, H_4), 4.04–4.25 (m, 1H, H_2), 4.45–4.55 (m, 2H, H_{10}), 4.6–4.75 (m, 1H, H_5), 6.47, 6.5 (d, 1H, J = 6 Hz, H_6); for hypoxanthine 7.97 (s, 2H, H_2), 8.18 (s, 2H, H_8), 12.32 (bs, 1H, NH). Elemental analysis calcd for $C_{11}H_{12}N_4O_2$ (**3b** or **4b**): C, 56.9; H, 5.17; N, 24.1%. Found: for **3b**; C, 56.55; H, 5.43; N, 24.25: for **4b**; C, 56.25; H, 5.5; N, 23.62%.

Table 1 Copolymerization of monomes with maleic anhydride (MA) in DMF at 90°C using AIBN as initiator

No.	Monomer ($mol l^{-1}$)	MA ($mol l^{-1}$)	Initiator ($mol l^{-1}$)	Time (h)	Yield (%)	Polymer M_n[a]	Polymer $[\eta]$[b] ($dl g^{-1}$)
	3a						
1	7.99	23.96	0.32	15	40.0	–	–
2	7.99	15.97	0.44	15	32.3	–	–
3	2.00	4.01	0.08	48	76.8	–	–
4	3.99	7.99	0.17	48	82.2	2400	0.022
	3b						
5	8.44	10.02	0.30	48	12.7	–	–
	3d						
6	1.94	3.87	0.12	48	25.2	–	–
	4a						
7	3.34	6.67	0.20	48	66.0	–	–
8	7.41	14.83	0.46	48	81.0	2900	0.031
	4b						
9	0.96	1.92	0.06	48	24.7	–	–

[a] Number-average molecular weights measured by g.p.c. in H_2O
[b] Intrinsic viscosity in H_2O at 30°C

*2-(6-Thioxo-1H-purin-9-ylmethyl)-3,4-dihydro-2H-pyran (**3c**).* Compound **3a** (0.7 g, 2.28 mmol) was dissolved in a mixture of ethanol (70 ml) and 2 N aqueous NaSH (70 ml) and this solution was stirred for 8 h at 80°C. Compound **3c** was precipitated by adjusting the solution to pH 6–7 with acetic acid in an ice bath, filtered, and then crystallized in methanol (0.32 g, m.p. 269°C (dec.), yield 46.2%).

^{1}H n.m.r. (200 MHz, DMSO-d_6), δ (ppm): for 2-methylhydropyran 1.4–1.65 (m, 1H, H_{3a}), 1.9–2.2 (m, 3H, H_{3b}, H_4), 4.1–4.3 (m, 1H, H_2), 4.31–4.5 (m, 2H, H_{10}), 4.7–4.8 (m, 1H, H_5), 6.33, 6.36 (d, 1H, $J = 6$ Hz,H_6); for 6-mercaptopurine 8.21 (s, 1H, H_2), 8.23 (s, 1H, H_8), 13.8 (bs, 1H, NH). Elemental analysis, calcd for $C_{11}H_{12}N_4OS$: C, 53.23; H, 4.84; N, 22.58; S, 12.9%. Found: C, 52.87; H, 5.09; N, 21.93; S, 12.39%.

*2-(Adenin-9-ylmethyl)-3,4-dihydro-2H-pyran (**3d**).* Compound **3a** was dissolved in 100 ml of saturated methanolic ammonia solution, and this solution was then heated in an autoclave at 75°C for 5 h. After evaporating the solvent, the residues were crystallized in ethanol to give 0.32 g of **3d** (m.p. 199–200°C, yield 45.8%).

^{1}H n.m.r. (200 MHz, DMSO-d_6), δ (ppm): for 2-methylhydropyran 1.35–1.6 (m, 1H, H_{3a}), 1.8–2.16 (m, 3H, H_{3b}, H_4), 4.05–4.28 (m, 1H, H_2), 4.3–4.43 (m, 2H, H_{10}), 4.6–4.8 (m, 1H, H_5), 6.33, 6.36 (d, 1H, $J = 6$ Hz, H_6); for adenine 8.1 (s, 1H, H_8), 8.15 (s, 1H, H_2), 7.25 (bs, 2H, NH_2). Elemental analysis, calcd for $C_{11}H_{13}N_5O$: C, 57.14; H, 5.63; N, 30.30%. Found: C, 56.82; H, 5.48; N, 30.33%.

Copolymerization and hydrolysis

The calculated amounts of monomers, solvents, and the initiator (AIBN) were charged into the polymerization tubes (*Table 1*), which were then immersed in a Dewar flask containing dry ice and acetone. After a number of freeze–thaw cycles under N_2, the tubes were then sealed and placed in an oil bath at 90°C for various periods of time as listed in *Table 1*. After diluting the polymerization solutions with DMF, polymers **5a** and **7a** were precipitated in acetone (twice), and then converted in to **6a** and **8a** by dissolving in water. The polymers were collected by freeze drying. The diluted polymerization solutions of **5b**, **5c** and **7b** were added to water to give **6b**, **6c**, and **8b**, respectively, and these were then dialysed through a membrane with a *MW* cut-off of 1000 and freeze dried. Polymers **6a** and **8a** were hydrolysed by stirring in 0.1 N NaOH for 2 h to give polymers **6b** and **8b**, respectively, which were purified by dialysis through a membrane as described above.

Hyper- or hypochromicity

U.v. spectra were recorded by using a Jasco V-550 spectrophotometer. The base residue concentrations in the solutions were 10^{-4} mol l^{-1}. The percentage hyper- or hypochromicity (h %) was calculated from equation (1) where ϵ_p and ϵ_m denote the molar extinction coefficients of the base residues of the polymers and the relevant monomers, respectively, at the wavelength of 250 nm. A positive value of h represents hyperchromicity whereas a negative value indicates hypochromicity.

$$h(\%) = 100[(\epsilon_p - \epsilon_m)/\epsilon_m] \quad (1)$$

Measurements

^{1}H and ^{13}C n.m.r. spectra were recorded on a Varian Gemini 200 spectrometer. I.r. spectra were obtained with a Perkin-Elmer Model 283B spectrophotometer. Fluorescence spectra were recorded on a Kontron Instrument SFM25 fluorescence spectrophotometer. Gel permeation chromatography (g.p.c.) was carried out by using a Waters 150-CV with a RI detector under the following conditions: a Waters ultrahydrogel 250 column with water or aqueous 0.1 N $NaNO_3$ at a flow rate of 0.8 ml min^{-1}.

Elemental analysis was carried out at the Korea Research Institute of Chemical Technology.

RESULTS AND DISCUSSION

Synthesis and characterization of monomers

2-(Tosyloxymethyl)-3,4-dihydro-2*H*-pyran (**2**) was prepared by the reaction of tosyl chloride with 2-(hydroxymethyl)-3,4-dihydro-2*H*-pyran, which was obtained by the reduction of 2-formyl-3,4-dihydro-2*H*-pyran, the Diels–Alder product of acrolein, with the aid of $NaBH_4$.

Owing to the poor solubility of hypoxanthine in organic solvents, 2-(hypoxanthin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3b**) could not be obtained by the direct reaction of hypoxanthine with **2**. Synthesis of the monomers was started with various 6-chloropurine derivatives in which the chloro groups can be easily replaced by hydroxy or amino groups, as shown in *Scheme 1*.

Alkylation of **1** with **2** produced both 7- and 9-substituted compounds, with the latter compound being the major product. 2-(6-Chloropurin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3a**), and its N(7)-isomer, 2-(6-chloropurin-7-ylmethyl)-3,4-dihydro-2*H*-pyran (**4a**), were separated by column chromatography.

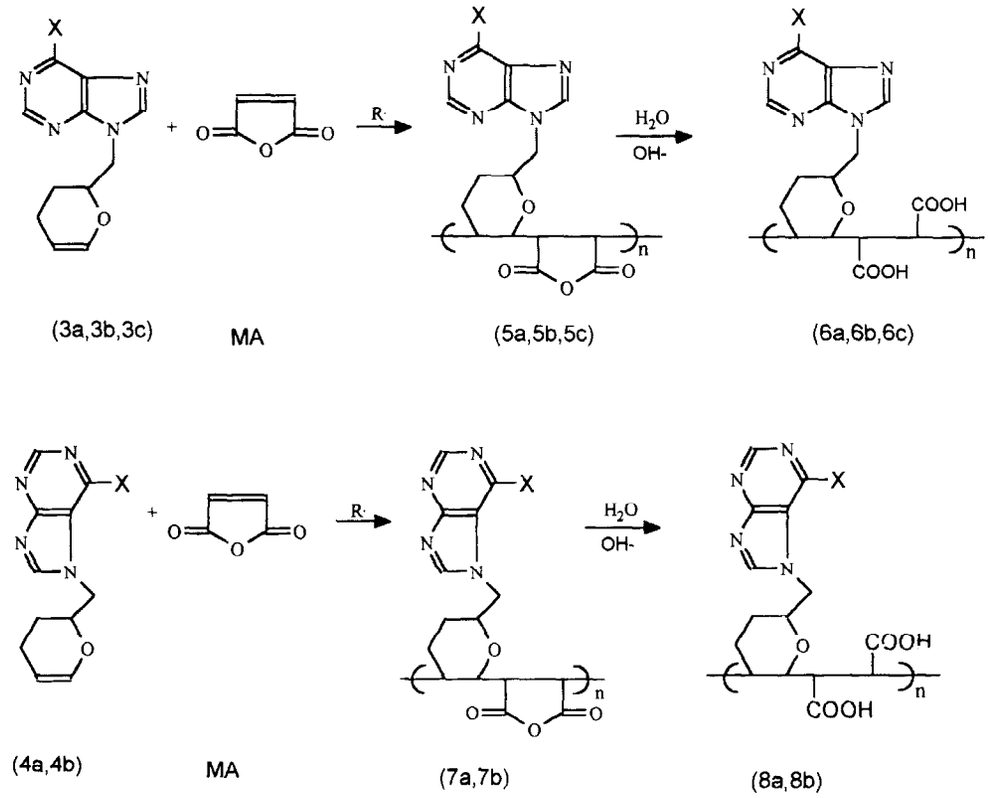
The structures of compounds **3a** and **4a** were confirmed by u.v. and n.m.r. spectroscopy. The u.v. spectral data for compound **3a** ($\lambda_{max} = 270.0$ nm, $\epsilon = 7200$) and compound **4a** ($\lambda_{max} = 272$ nm, $\epsilon = 6260$) were coincident with the result that N(9)-alkylated compounds of purine derivatives showed maximum u.v. absorptions at shorter wavelengths, with higher extinction coefficients, than those of the N(7)-isomers[29]. The ^1H and ^{13}C n.m.r. data of compounds **3a** and **4a** (given in the Experimental section) were also in agreement with the result that the signals of H8 for the N(9)-isomers were shifted upfield relative to the corresponding H8 signals for the N(7)-isomers, while the ^{13}C peaks of the bridge carbon atoms ($-N-CH_2-$) of the N(9)-isomers were shifted upfield relative to the relevant peaks of the N(7)-isomers[30].

Compounds **3a** and **4a** were treated with aqueous trimethylamine to convert them into 2-(hypoxanthin-9-ylmethyl)-2,3-dihydro-2*H*-pyran (**3b**) and 2-(hypoxanthin-7-ylmethyl)-2,3-dihydro-2*H*-pyran (**4b**), respectively, with the latter being identified by the appearance of amide band a at 1725 and 1690 cm^{-1} in the i.r. spectra and of proton signals for the amide group at $\delta = 12.32$ and 12.38 ppm in the ^1H n.m.r. spectra of compounds **3b** and **4b**, respectively.

Compound **3a** was also treated with sodium hydrosulfide to give 2-(6-mercaptopurin-9-yl methyl)-3,4-dihydro-2*H*-pyran, which was so unstable as to be immediately transformed in to its desmotropic form, 2-(6-thioxo-1*H*-purin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3c**). This was confirmed by the appearance of a thioamide proton at $\delta = 13.8$ ppm, as well as the absence of mercaptan protons in the ^1H n.m.r. spectrum of **3c**. By treating **3a** with methanolic ammonia, it was converted to 2-(adenin-9-ylmethyl)-3,4-dihydro-2*H*-pyran (**3d**).

Copolymerization and hydrolysis

The radical copolymerization of 3,4-dihydro-2*H*-pyran derivatives with maleic anyhdride (MA) is



Scheme 2

known to give alternating copolymers by forming charge-transfer complexes of the monomer pairs during the copolymerization reaction[27–29]. As the electron donating character of the cyclic vinyl ether groups of compounds **3** and **4** is influenced to a negligible extent by substitutions on the C(2) position of the dihydropyran rings, copolymerization of these compounds with maleic anhydride will result in alternating copolymers, such as poly[(2-(6-chloropurin-9-ylmethyl)-3,4-dihydro-2*H*-pyran)-*alt*-(maleic anhydride)] (**5a**), poly[(2-(hypoxanthin-9-yl methyl)-3,4-dihydro-2*H*-pyran)-*alt*-(maleic anhydride)] (**5b**), poly[(2-(6-thioxo-1*H*-purin-9-ylmethyl)-3,4-dihydro-2*H*-pyran)-*alt*-(maleic anhydride)] (**5c**), poly[(2-(6-chloropurin-7-ylmethyl)-3,4-dihydro-2*H*-pyran)-*alt*-(maleic anhydride)] (**7a**), and poly[(2-(hypoxanthin-7-ylmethyl)-3,4-dihydro-2*H*-pyran)-*alt*-(maleic anhydride)] (**7b**).

The copolymerizations of compounds **3** and **4** with maleic anhydride (MA) have been carried out in dimethylformamide in the presence of the radical initiator (AIBN) and the copolymerization data are given in *Table 1*. Although copolymerization in bulk was expected to give high yields, this could not be carried out due to the high melting points of compounds **3** and **4**. Neither the dihydropyran derivatives **3** and **4**, nor maleic anhydride were homopolymerized under the same conditions, and hence the resulting copolymers should have alternating sequences.

The yields of the polymers (*Table 1*) increased with increasing monomer concentration at the start of the copolymerization and polymerization periods. The low molecular weights of the copolymers (see *Table 1*) are attributable to various transfer reactions which often occurred in the polymerization of the cyclic vinyl ether monomers[23,25], as shown in *Scheme 3*. The allyl and/or allyloxy radicals, formed by hydrogen transfer from the monomer to the radical active centre, are very stable due to the formation of resonance hybrids. These stable radicals can start the copolymerization anew. This point was confirmed by the presence of the peaks at 6.36 and 4.71 ppm in the ^{1}H n.m.r. spectra of copolymers **5** and **7**, corresponding to H6 on the dihydropyran rings, indicating the presence of trace amounts of vinyl protons.

After isolation of the polymers **5a** and **7a**, they were hydrolysed to give poly[(2-(6-chloropurin-9-yl methyl)-tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)] (**6a**) and poly[(2-(6-chloropurin-7-yl methyl)tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)] (**8a**), respectively. Owing to their poor solubilities in organic solvents, polymers **5b**, **5c**, and **7b** were directly subjected to hydrolysis to give poly[(2-(hypoxanthin-9-yl methyl)tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)] (**6b**), poly[(2-(6-thioxo-1*H*-purin-9-ylmethyl)tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)] (**6c**), and poly[(2-(hypoxanthin-7-yl methyl) tetrahydropyran-5,6-diyl) (1,2-dicarboxyethylene)] (**8b**), which were purified by dialysis. The hydrolysis of the anhydride groups was monitored by i.r. spectroscopy in which the cyclic anhydride peak at 1825 cm^{-1} in the spectra disappeared, while carboxylate groups at 1730 cm^{-1} emerged.

The ^{1}H n.m.r. spectra of polymer **6b** and monomer **3b** are shown in *Figure 1*. In the n.m.r. spectrum of **6b**, the proton signals of C(2) and C(8) in the hypoxanthinyl groups appeared at 7.9–8.8 ppm and those of the backbone of the polymer at 1–5.5 ppm. The ratio of the integration values was found to be ~2–11, which coincided with the alternating structure of the copolymer.

Base-stacking

According to both the Tinoco[30] and Rhodes[31] theories, induced dipole–dipole interactions in the chromophores of nucleic acids can result in either hypochroism or hyperchroism, depending on the relative geometry of the stacked chromophores. Hypochroism is common to those systems where the chromophores are stacked one upon another like a deck of cards, while systems in which the chromophores are situated in an end-to-end aggregate are generally predicted to be hyperchromic.

The u.v. spectra of monomer **3b** and polymer **6b** are shown in *Figure 2*. The base stacking of the nucleic acids was investigated by examining the u.v. absorption at wavelength of 250 nm. Polymer **6b** (ϵ = 8240) showed 23.7% of hypochromicity in comparison with the u.v. absorption of the corresponding monomer **3b** (ϵ = 10 800).

The carboxylate groups of polymer **6b** at a pH of 7 in aqueous solution are likely to protrude outward, thus interacting with the hydrophilic environment, and hence the guanyl bases seemed to result in stacking. The

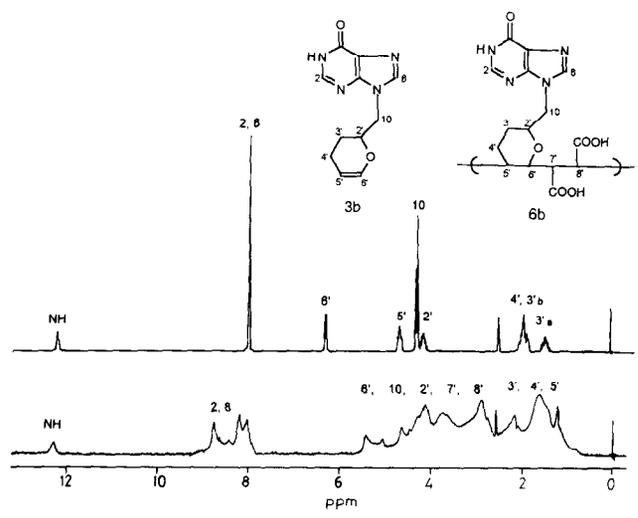
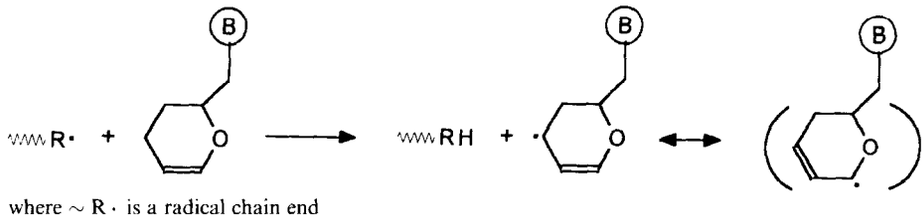


Figure 1 ^{1}H n.m.r. spectra of monomer **3b** in DMSO-d_6 (upper curve) and polymer **6b** (lower curve) in D_2O



where ~ R · is a radical chain end

Scheme 3

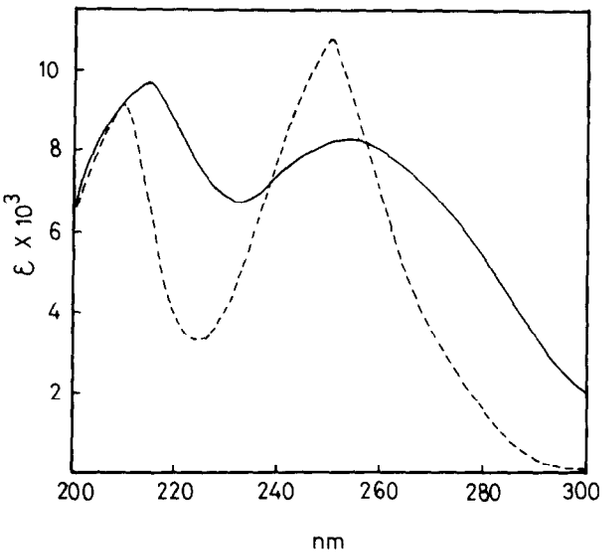


Figure 2 U.v. spectra of monomer **3b** (dotted line) and polymer **6b** (solid line) in H_2O

hypochromicity observed in this system can be attributed to the geometry of the stacked chromophores; the transition dipoles of the hypoxanthinyl groups of polymer **6b** seemed to be aligned parallel. Polymer **8b** also showed hypochromicity, by comparison with the u.v. absorption of monomer **4b**.

Excimer fluorescence

Bichromophoric molecules in which the two aromatic chromophores are separated by a three-atom linkage, give rise to intramolecular excimer formation[32–34]. Excimer formation in these systems requires rotational motion about the bond of the linkage to allow the two chromophores to reach, within the lifetime of the excited state, a conformation suitable for complex formation in which the two aromatic rings overlap in a sandwich-like arrangement. When these geometrical requirements are satisfied for the pendant chromophores on the polymer chains, the polymer shows an excimer fluorescence as observed in poly(vinyl aromatics)[33,35–38] and polymers containing chromophoric pendant groups[39]. Therefore, the excimer fluorescence can provide additional evidence for base-stacking in the polynucleotide analogues.

The fluorescence emissions of compound **4b** and polymer **8b** at 20°C, after excitation at 250 nm, were measured at the same concentrations of hypoxanthinyl groups (1×10^{-5} residue mol l^{-1}) in H_2O (*Figure 3*). Compound **4b** showed a broad peak at 400 nm with very low intensity, whereas **8b** gave a broad band at 422 nm with very high intensity. The fluorescense emission of the polymer was red-shifted relative to the emission band from compound **4b**, and was devoid of vibrational structures. These are typical characteristics for the excimer fluorescence, indicating that the chromophores of the polymer formed excimers in aqueous solutions. Polymer **6b** showed the same trend as polymer **8b**.

Polyelectrolyte behaviour

Polymers **6** and **8** are polyelectrolytes. The hydrodynamic volume of the polyelectrolyte increases greatly in a dilute aqueous solution. The polyelectrolyte expansion effect is strongly dependent on the ionic strength of the solution and is successfully suppressed in 0.1 N $NaNO_3$ aqueous solution, which was confirmed by the universal calibration method[40,41].

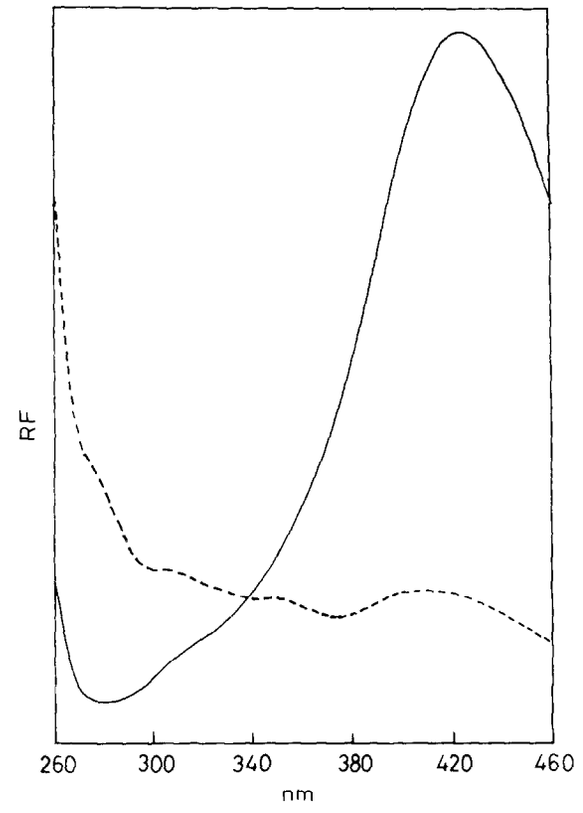


Figure 3. Fluorescence emission spectra of monomer **4b** (dotted line) and polymer **8b** (solid line) in H_2O after excitation at 253 nm

The molecular weights of polymers **6b** and **8b** were measured by gel permeation chromatography at room temperature. The number-average molecular weights of polymers **6b** and **8b** were found to be 2400 and 2900, respectively. The reduced viscosities of polymer **8b**, as a function of concentration in H_2O are shown in *Figure 4*. They exhibit typical polyelectrolyte behaviour in which the reduced viscosity decreases at the beginning and thereafter increases sharply with continuous dilution. After the addition of neutral salts they retain normal behaviour (*Figure 4*).

CONCLUSIONS

We have prepared the novel polynucleotide analogues **6** and **8** containing hypoxanthine, 6-chloropurine, and 6-mercaptopurine bases. These PNAs were soluble in water and contained alternating sequences between the nucleoside analogues and dicarboxyethylene groups along the polymer chains. They showed physico-chemical properties which were quite similar to those of the natural polymers, such as hypochromicity and polyelectrolyte behaviour. Polymer **6b**, for example, showed 23.7% of hypochromicity of the u.v. absorption at a wavelength of 250 nm in aqueous solutions. Polymer **8b** in an aqueous solution showed broad excimer fluorescence around 422 nm at 20°C, which was found to be red-shifted relative to the emission from the monomer and devoid of vibrational structures. Due to polyelectrolyte effects, the reduced viscosities measured in an aqueous solution decreased at the beginning and thereafter increased sharply with continuous dilution.

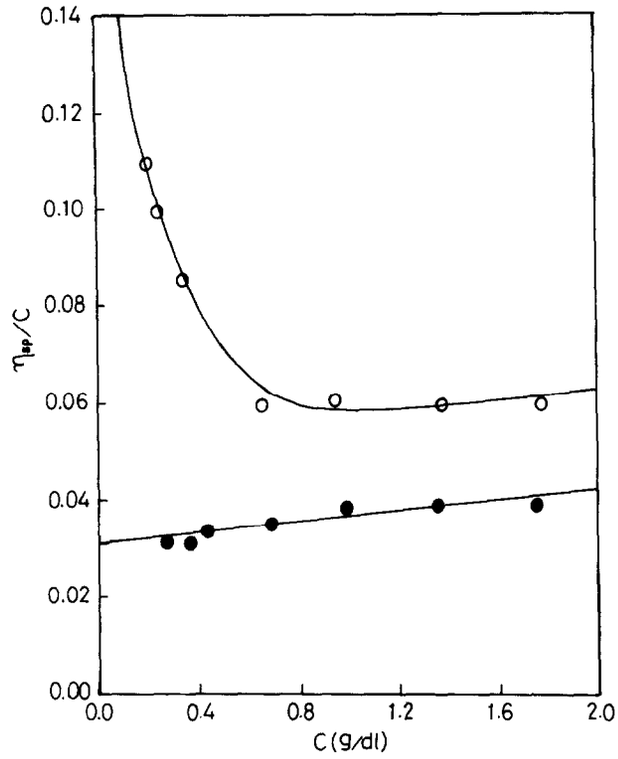


Figure 4 Reduced viscosities of the sodium salt of polymer **8b** in H_2O (upper curve) and aqueous 0.1 N $NaNO_3$ solution (lower curve)

ACKNOWLEDGEMENT

This work was supported by a grant from the Korea Science and Engineering Foundation.

REFERENCES

1 Kondo, K., Iwasaki, H., Ueda, N., Takemoto, K. and Imoto, M. *Makromol. Chem.* 1968, **120,** 21
2 Kaye, H. *Polym. Lett.* 1969, **7,** 1
3 Kondo, K., Iwasaki, H., Nakatani, K., Ueda, N., Takemoto, K. and Imoto, M. *Makromol. Chem.* 1969, **125,** 42
4 Kondo, K., Hisaoka, Y. and Takemoto, K. *Chem. Lett.* 1973, 125
5 Kita, Y., Inaki, Y. and Takemoto, K. *J. Polym. Sci. Polym. Chem. Edn* 1980, **18,** 427
6 Kondo, K. and Takemoto, K. *Makromol. Chem. Rapid Commun.* 1980, **2,** 203
7 Anand, N., Murthy, N. S. R. K., Naider, F. and Goodman, M. *Macromolecules* 1971, **4,** 564
8 Saita, T., Yamauchi, K., Kinoshita, M. and Imoto, M. *Makromol. Chem.* 1972, **154,** 263
9 Saita, T., Yamauchi, K., Kinoshita, M. and Imoto, M. *Makromol. Chem.* 1973, **163,** 15
10 Ishigawa, T., Inaki, Y. and Takemoto, K. *Polym. Bull.* 1978, **1,** 85
11 Overberger, C. G. and Inaki, Y. *J. Polym. Sci. Polym. Chem. Edn* 1979, **17,** 1739
12 Overberger, C. G. and Morishima, Y. *J. Polym. Sci. Polym. Chem. Edn* 1980, **18,** 1247
13 Ludwick, A. and Overberger, C. G. *J. Polym. Sci. Polym. Chem. Edn* 1982, **20,** 123
14 Overberger, C. G. and Lu, C. X. *J. Polym. Sci. Polym. Chem. Edn* 1986, **24,** 243
15 Overberger, C. G. and Lu, C. X. *J. Polym. Sci. Polym. Chem. Edn* 1987, **25,** 1523
16 Overberger, C. G. and Chang, J. Y. *J. Polym. Sci. Polym. Chem. Edn* 1989, **27,** 3589
17 Overberger, C. G., Chang, J. Y. and Gunn, E. V. *J. Polym. Sci. Polym. Chem. Edn* 1989, **27,** 99
18 Overberger, C. G. and Chang, J. Y. *J. Polym. Sci. Polym. Chem. Edn* 1989, **27,** 4013
19 Halford, M. H. and Jones, A. S. *J. Chem. Soc.* 1968, 2667
20 Buttrey, J. D., Jones, A. S. and Walker, R. T. *Tetrahedron* 1975, **31,** 73
21 Ishiwara, T., Inaki, Y. and Takemoto, K. *Polym. Bull.* 1978, **1,** 215
22 Han, M. J. and Park, S. M. *Macromolecules* 1990, **23,** 5295
23 Han, M. J., Lee, C. W., Kim, K. H. and Lee, S. H. *Macromolecules* 1992, **25,** 3528.
24 Han, M. J., Park, S. M., Park, J. Y. and Yoon, S. H. *Macromolecules* 1992, **25,** 3534
25 Han, M. J., Chang, Y. S., Park, J. Y. and Kim, K. H. *Macromolecules* 1992, **25,** 6574
26 Han, M. J., Kim, K. S., Cho, T. J., Kim, K. H. and Chang, J. Y. *Macromolecules* 1994, **27,** 2896
27 Han, M. J., Kim, K. H., Cho, T. J. and Choi, K. B. *J. Polym. Sci. Polym. Chem. Edn* 1990, **28,** 2719
28 Han, M. J., Choi, K. B., Chae, J. P. and Hahn, B. S. *J. Bioactive Compatible Polym.* 1990, **5,** 80
29 Han, M. J., Choi, K. B., Chae, J. P. and Hahn, B. S. *Bull. Korean Chem. Soc.* 1990, **11,** 154
30 Tinoco, Jr. I. *J. Am. Chem. Soc.* 1961, **83,** 5047
31 Rhodes, W. *J. Am. Chem. Soc.* 1961, **83,** 3609
32 Browne, D. T., Eisinger, J. and Leonard, N. J. *J. Am. Chem. Soc.* 1968 **90,** 7302
33 Inaki, Y., Renge, T., Kondo, K. and Takemoto, K. *Makromol. Chem.* 1975, **176,** 2683
34 Hirayama, F. *J. Chem. Phys.* 1965, **42,** 3163
35 MacDonald, J. R., Echols, W. E., Price, T. R. and Fox, R. B. *J. Chem. Phys.* 1972, **57,** 1746
36 Ishii, T., Handa, T. and Matsunaga, S. *Makromol. Chem.* 1977, **178,** 2351
37 Fox, B., Cozzens, R. F. and McDonald, J. R. *J. Chem. Phys.* 1972, **57,** 534
38 Yokoyama, M., Tamamura, T., Nakano, T. and Mikawa, H. *Chem. Lett.* 1972, 499
39 Itaya T., Ochiai, H., Ueda, K. and Imamura, A. *Macromolecules* 1993, **26,** 6021
40 Grubisic, Z., Rempp, P. and Benoit, H. *J. Polym. Sci. (C)* 1967, **5,** 753
41 Hamielec, A. and Styring, M. *Pure Appl. Chem.* 1985, **57,** 955