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Synthesis of Polyacrylic and Polymethacrylic Derivatives Having Pendant Uracil and Thymine Moieties

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Summary

Polyacrylic and polymethacrylic derivatives containing different contents of pendant uracil and thymine units were prepared by the polymeranalogous reaction using cyclic derivatives of uracil and thymine. The ability of the interaction between thymine bases in the copolymer chain was found to be parallel to the thymine content.

Introduction

Cyclonucleosides are valuable intermediate compounds for synthesizing various nucleoside derivatives (COHEN 1966). As a model of the cyclonucleosides, cyclic compounds of uracil (2a) and thymine (2b) were prepared (INAKI et al. 1979). These cyclic derivatives showed similar reactivity as the cyclonucleosides against a number of reagents, and were substantially useful as intermediate compounds for the preparation of pyrimidine derivatives (AKASHI et al. 1977).

The present paper deals with a new method for preparing the polymers having pendant nucleic acid bases by the polymeranalogous reaction of the cyclic compounds (2a, 2b) with polyacrylic and polymethacrylic acids. By this method, a series of polymers containing different amounts of pyrimidine bases can be easily prepared.

Experimental

Cyclic derivatives of uracil (2a) and thymine (2b).

The cyclic derivatives, that is, 1,2-O-ethanouracil and 1,2-O-ethanothymine (2a, 2b) were prepared from their corresponding chloroethyl derivatives (1a, 1b) by dehydrochlorination with 1,8-diaza-bicyclo(5,4,0)-undecene-7 (DBU)(INAKI et al. 1979)(Scheme 1).

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Polymer reaction of polyacrylic acid with the cyclic compounds.

To a suspension of polyacrylic acid (1.44 g, 20 mmol) in N,N-dimethylformamide (DMF)(30 ml), 2b (3.04 g, 20 mmol) was added at 80°C with stirring. The suspension became a clear solution after few days. After stirring further 10 days, the solvent was distilled off under reduced pressure. Excess acetone was then added to the oily residue obtained to give precipitate of the polymer. Reprecipitation from DMF-acetone gave the polymer (3b) in a quantitative yield.

Polyacrylic derivatives having different contents of thymine and uracil (3a), and polymethacrylic derivatives having different contents of uracil and thymine (4a, 4b) were also prepared using a similar procedure described above.

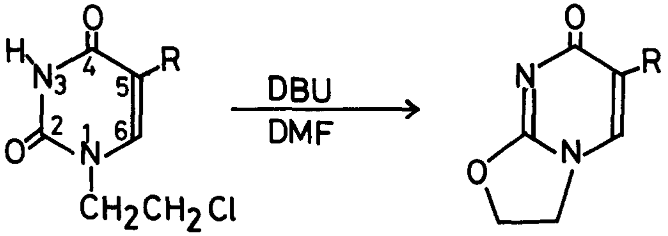
Hydrolysis of copolymers

The contents of the pyrimidine base in the copolymers obtained were determined by measuring UV absorbance of the product after hydrolysis. Hydrolysis of the copolymer was carried out by 10 N-hydrochloric acid at room temperature for 2 days, which gave oxyethyl derivatives of uracil and thymine as well as polyacrylic or polymethacrylic acid. The authentic polymethacryloyloxyethylthymine was confirmed to be hydrolyzed to give oxyethylthymine with 98 % yield. For the quantitative calculation, the authentic oxyethyl derivatives of uracil or thymine were used.

Results and Discussion

A series of polyacrylic and polymethacrylic derivatives having uracil and thymine moieties were prepared as shown in Scheme 2.

Scheme 1.



(1)

R: H (1a); CH_3 (1b)

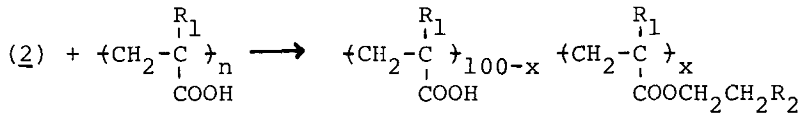
(2)

R: H (2a); CH_3 (2b)

Cyclic derivatives of uracil (2a) and thymine (2b) were obtained in high yield from the corresponding chloroethyl derivatives (1a, 1b) by dehydrochlorination with DBU in DMF solution. Structure of 2a and 2b was identified by NMR, IR, UV and mass spectra, as well as elemental analysis (INAKI et al. 1979).

Reactions of the cyclic compounds with different kinds of reagents gave pyrimidine derivatives conveniently at room temperature without catalyst. One of the typical reaction is the esterification by acetic acid in bulk, which affords the corresponding acetate. When this reaction was applied to polymeric acids, that is, polyacrylic and polymethacrylic acids, polyacrylate and polymethacrylate having pendant uracil and thymine were obtained in high yield (Scheme 2).

Scheme 2.



$$(2) + \left(CH_2-\overset{R_1}{\underset{COOH}{C}} \right)_n \longrightarrow \left(CH_2-\overset{R_1}{\underset{COOH}{C}} \right)_{100-x} \left(CH_2-\overset{R_1}{\underset{COOCH_2CH_2R_2}{C}} \right)_x$$

(3)

R_1 \ R_2	Uracil	Thymine
H	p-AOU-x (3a)	p-AOT-x (3b)
CH_3	p-MAOU-x (4a)	p-MAOT-x (4b)

By using this reaction, copolymers of acrylic acid and N-β-methacryloyloxyethyl derivative of uracil or thymine, and also those of methacrylic acid and the methacrylate of the pyrimidine bases were successfully prepared, which had the same degree of polymerization as the original polyacrylic and polymethacrylic acids. A series of the copolymers was obtained by varying the molar ratio of the cyclic compound to the polymeric acid. Molecular weight of polyacrylic and polymethacrylic acids used here was about 15,000.

The content of pyrimidine base in the copolymer was determined by measuring UV absorbance of the oxyethyl derivative of the pyrimidine base which was obtained by hydrolysis of the copolymer. The analytical data are listed in Table 1. The table shows that the cyclic compound reacted almost quantitatively with polyacrylic and polymethacrylic acid. From NMR, IR and UV spectra, the polymer having the highest content of the pyrimidine base was found to be identical to the authentic homopolymer which was prepared by free

Table 1. Synthesis of the Copolymers

Copolymer	Base content	
	Calcd. (%)a)	Found (%)b)
p-AOU-100	100	90c)
p-AOT-100	100	87
- 75	75	65
- 50	50	36
- 25	25	19
- 10	10	7.4
- 5	5	4.0
p-MAOU-100	100	100c)
p-MAOT-100	100	100c)
- 80	80	69
- 60	60	44
- 40	40	37
- 20	20	19
- 10	10	7.9
- 5	5	3.9

a) Mol % of the cyclic compound (**2**) used for the polymer reaction to the total concentration of carboxylic acid groups.
b) Uracil or thymine contents in the copolymer after the reaction (unit mol %).
c) Base content measured from NMR spectra.

Table 2. UV Spectra of the Copolymers

Copolymer	ε_{max}a)	Hypochromicity(%)b)
p-AOT-100	8100	13
- 75	8200	12
- 50	8200	12
- 25	8400	9.7
- 10	8600	7.5
- 5	8700	6.5
p-MAOT-80	8200	12
-60	8300	11
-40	8500	8.6
-20	8600	7.5
-10	8700	6.5
- 5	8700	6.5
T-T	17300	7.0
T-M	9300	0

a) λ_{max} = 270.5 nm, in DMF solution at 25°C.
b) Hypochromicity based on T-M.

radical polymerization of the corresponding vinyl monomer.

The UV spectra of the copolymers in DMF solution are listed in Table 2. From the data, percent hypochromicity of the polymers was estimated and listed also in the same table. This table contains further the data of the dimer (T-T) and the monomer (T-M) model compounds reported previously (KITA et al. 1979). In both p-AOT and p-MAOT series, the value of hypochromicity decreases with decreasing the thymine content, and becomes to be closely near the value of the dimer model compound. From the data, it is suggested that the thymine bases in the copolymer can interact each other, and the ability of the interaction tends to be parallel to the thymine content.

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