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α-Chloromaleic Anhydride–Allylcyclohexane Copolymer and Its Dehydrochlorination

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The interaction of α-chloromaleic anhydride (ClMAn) and allylcyclohexane (ACH) was studied. These monomers were found to make a charge-transfer (CT) complex at a 1 : 1 ratio. Copolymerization of ClMAn and ACH in solution gave a white powder in about 50% yield of which analytical data suggested that ClMAn and ACH are copolymerized in a 1 : 1 ratio. By heating the copolymer at 190 °C for 1 h under reduced pressure, dehydrochlorination occurred quantitatively to generate a double bond in the polymer chain at the position of maleic anhydride moiety. The dehydrochlorinated copolymer was found to make a CT complex with acetone but the value of the formation constant was smaller than that of monomeric maleic anhydride.

Keywords α-chloromaleic anhydride; allylcyclohexane; charge-transfer complex; copolymerization; dehydrochlorination; formation constant

It is important to elucidate the mutual interaction between a polymer and substrates to develop a polymeric drug. Maleic anhydride (MAn) forms charge-transfer (CT) complexes with many compounds where MAn acts as an electron acceptor. On the other hand, MAn is known to copolymerize with various other monomers,[1—7] and the acid anhydride moiety introduced in the copolymer has been successfully used for immobilization of enzymes[8—10] and macromolecular prodrug.[11] Only a few reports have been made, however, on the copolymerization of the α-substituted maleic anhydride derivative.[12—15] α-Chloromaleic anhydride (ClMAn) forms a CT complex with styrene and the copolymerization of the monomers has been studied to give the alternating copolymer.[14] Dehydrochlorination of the chlorosuccinic anhydride moiety in the copolymer may give a structure similar to MAn in the polymer chain, and the MAn moiety thus introduced forms CT complexes with acetone as well as monomeric MAn. As the polymer retains the benzene ring arising from styrene, the benzene ring also seems to form a CT complex with substrates.

Using allylcyclohexane (ACH) which has no benzene ring, the copolymerization of ClMAn and ACH was studied. The dehydrochlorination for introduction of the MAn moiety in the ClMAn and ACH copolymer (ClMAn–ACH) was then investigated. The interaction of the dehydrochlorinated copolymer (deClMAn–ACH) with substrates was also examined.

Experimental

The IR spectra were recorded on a JASCO IR Report-810 spectrophotometer using KBr disks and the NMR spectra were taken on a JNM-EX90 or a JNM-GSX400 FT NMR. The NMR sample solutions were prepared in $CDCl_3$ with a small amount of tetramethylsilane as an internal reference. The absorption spectra were obtained at 25 °C by a Shimadzu UV-160 spectrophotometer, using a cell with a path length of 1 cm. The concentration expressed as [deClMAn–ACH] in the spectrophotometric study represents the molar concentration of MAn moiety based on the deClMAn–ACH. The carbon and hydrogen contents of the copolymers were determined at the Analytical Center, College of Science and Technology, Nihon University. Thermal behavior (thermogravimetry (TG) and differential thermal analysis (DTA)) were examined by TG–DTA (Rigaku) in nitrogen atmosphere with an increasing rate of 5 °C per minute. The molecular weight distributions[16,17] for the polymers were determined by gel permeation chromatography using high performance liquid chromatography column (Asahipak GF-7M HQ, Asahi Chemical Industry, Co., Ltd.) and tetrahydrofuran as the mobile phase at 25 °C. Intrinsic viscosities of the copolymers in chloroform were measured using an Ubbelohode-type viscometer at 25 °C.

Materials ClMAn (Wako Pure Chemical Industries, Ltd.) and ACH were purified by distillation under reduced pressure. Benzene, *n*-hexane, acetone, methylethylketone, and methylvinylketone were dried over sodium sulfate and purified by distillation. Chloroform was successfully washed with conc. sulfuric acid to remove organic impurities and water, and then dried in anhydrous calcium chloride and distilled before use. All other chemicals were of reagent grade.

Copolymerization of ClMAn and ACH ClMAn (13.25 g) and ACH (12.42 g) were polymerized in 360 ml of benzene in the presence of 0.10 g of benzoyl peroxide at 80 °C for 9 h under a nitrogen atmosphere. After polymerization, the reaction mixture was cooled to room temperature and was then added to 400 ml of *n*-hexane to obtain a white powdery precipitate. It was washed with *n*-hexane and dried *in vacuo* at 60 °C to give a constant weight. Twelve grams of copolymer was obtained. The weight-average molecular weight (M_w), the number-average weight (M_n), and the polydispersity (M_w/M_n) of the ClMAn–ACH were 2.92×10^3, 1.58×10^3, 1.85, respectively. Intrinsic viscosity ([η]): 0.033 dl/g. ^{13}C-NMR ($CDCl_3$) δ: a; 56.2 (CH),[18] b; 68.6 (CCl), c, d; 167.9 or 168.8 (CO) (a—d: see Chart 1).

Dehydrochlorination The ClMAn–ACH was heated at various temperatures for 1 h under reduced pressure. After the dehydrochlorination, the copolymer was dissolved in benzene and precipitated in a similar manner. The chlorine content in the copolymer was determined by the oxygen combustion method. The double bond introduced and carboxylic anhydride were analyzed in the usual way.[19] M_w, M_n, and M_w/M_n of the deClMAn–ACH (dehydrochrorinated at 190 °C for 1 h) were 2.88×10^3, 1.93×10^3, 1.49, respectively. [η] of the deClMAn–ACH: 0.041 dl/g. ^{13}C-NMR ($CDCl_3$) of the deClMAn–ACH δ: e, f; 142.6 or 147.6 (C=C), g, h; 163.9 or 165.2 (CO) (e—h: see Chart 1).

Results and Discussion

The copolymers, ClMAn–ACH and deClMAn–ACH, were prepared according to the pathway shown in Chart 1.

Equilibrium of the ClMAn and ACH Figure 1 shows the continuous variation curve[20,21] of the change in the NMR-chemical shift of α-position of ClMAn in chloroform. A maximum appeared at a 1 : 1 molar ratio of the coordinated ACH to ClMAn, that is, a CT complex with the molar ratio of ACH to ClMAn of 1 : 1 exists in the polymerization solution.

Introduction of MAn Moiety by Dehydrochlorination of ClMAn–ACH Figure 2 shows the thermal behavior of ClMAn–ACH examined by TG–DTA. The TG curve is scarcely changed up to about 170 °C, however, it shows a significant weight loss above 190 °C and an endothermic peak corresponding to this weight loss is observed around 190 °C. This weight loss suggests that the change in the

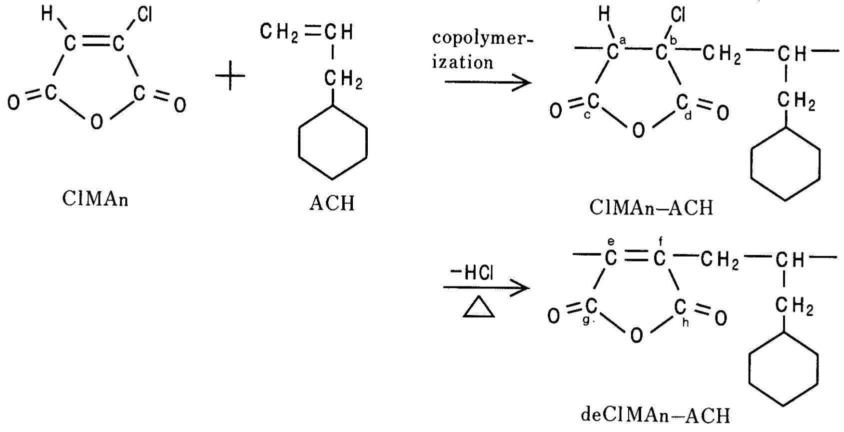

Chart 1

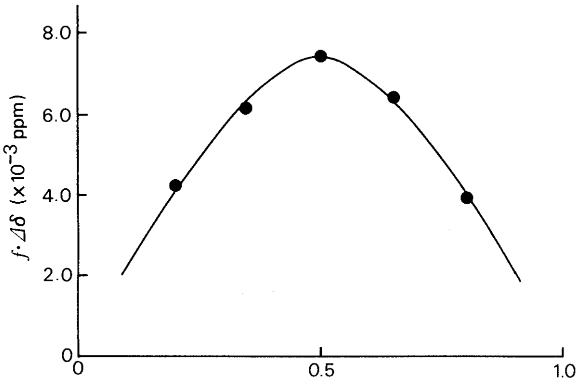

Fig. 1. Continuous Variation Method Applied to CT Complex for ClMAn–ACH System in Chloroform

[ClMAn]+[ACH]=0.25 (mol·dm^{-3}).

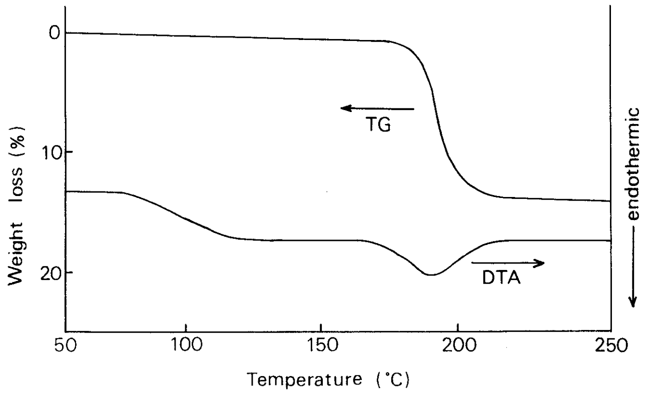

Fig. 2. TG–DTA Curves for ClMAn–ACH

TG–DTA around 190 °C is due to the decomposition of the copolymer. The weight loss by heating the ClMAn–ACH from 50 to 250 °C is 14.0% and this value is in good agreement with the calculated value (14.2%) based on complete removal of hydrogen chloride from the ClMAn–ACH, which is assumed to be an alternating copolymer. An endothermic change of the copolymer in the DTA curve around 90 °C was again observed after the copolymer was once heated to 250 °C, so the change around 90 °C may be attributed to the glass transition.

Table I shows the results of elemental analyses after heating the ClMAn–ACH for 1 h *in vacuo*. The chlorine content (13.7%) in the copolymer is in agreement with the calculated value (13.8%) based on the assumption that the copolymer is an alternating copolymer. The chlorine content in the copolymer on heating for 1 h at 130, 150, and 190 °C decreased to 9.7, 1.9, and 0%, respectively. The values in parentheses are the calculated values based on the chlorine content in the copolymer and are in close agreement with the data found.

Table I. Dehydrochlorination of ClMAn–ACH

Condition	Analysis (%)		
	C	H	Cl
—	59.6 (60.9)	6.5 (6.7)	13.7
130 °C, 1 h	63.9 (63.8)	6.8 (6.9)	9.7
150 °C, 1 h	69.1 (69.5)	7.1 (7.2)	1.9
190 °C, 1 h	70.6 (70.9)	7.3 (7.3)	0

Values in parentheses indicate the calculated value based on Cl content.

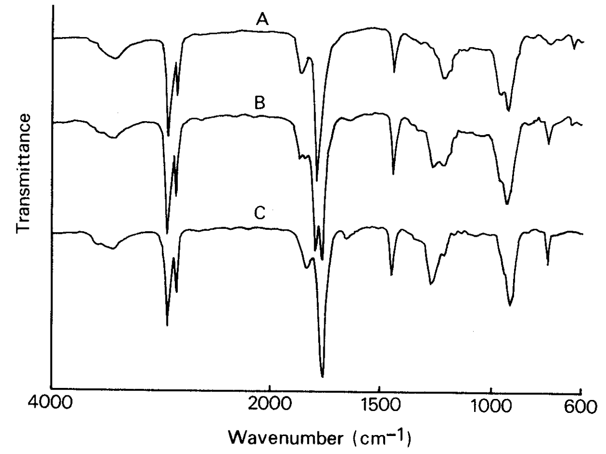

Fig. 3. IR Spectra of Copolymers

A, ClMAn–ACH; B, Copolymer obtained by heating of ClMAn–ACH at 130°C for 1 h; C, Copolymer (deClMAn–ACH) obtained by heating of ClMAn–ACH at 190°C for 1 h.

Figure 3 shows the typical changes in IR spectra on the progress of dehydrochlorination of the copolymer at 130 and 190 °C for 1 h. The initial ClMAn–ACH (A) shows the characteristic absorption bands at 1795 and 1865 cm^{-1} for acid anhydride and 650 cm^{-1} (C–Cl). When the copolymer

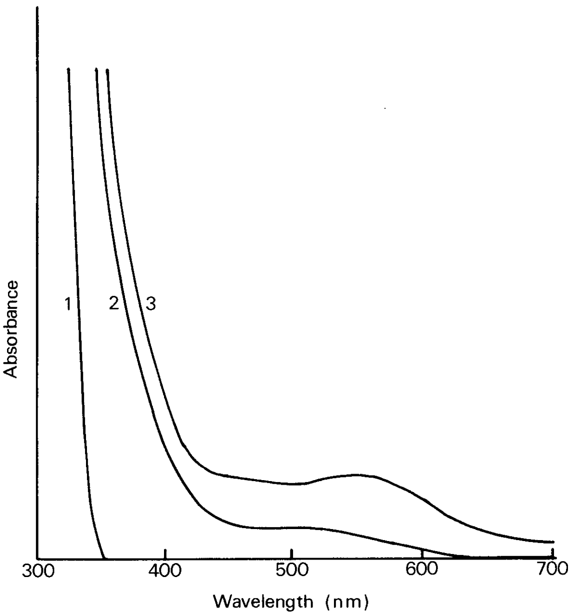

Fig. 4. Absorption Spectra for deClMAn–ACH Copolymer–Acetone System in *n*-Hexane

1, [acetone] = 10.0 (mol·dm^{-3}); 2, [acetone] = 2.5 (mol·dm^{-3}), [deClMAn–ACH] = 0.01 (mol·dm^{-3}); 3, [acetone] = 10.0 (mol·dm^{-3}), [deClMAn–ACH] = 0.01 (mol·dm^{-3}).

was heated at 190 °C for 1 h (C), the absorption band for acid anhydride shifted to 1765 and 1830 cm^{-1}, the absorption band for C=C appeared at 1650 cm^{-1} and C–Cl (650 cm^{-1}) disappeared. The copolymer heated at 130 °C (B) showed intermediate absorption bands between copolymer (A) and (C).

The structure of deClMAn–ACH was assigned as shown in Chart 1 by the analysis of its ^{13}C-NMR presented in the experimental section.

It is suggested that the copolymer from ClMAn and ACH is composed of the same molar ratio of these monomers, and the copolymer retaining structure similar to MAn moiety in the polymer chain is easily obtained by dehydrochlorination of the copolymer by heating for 1 h at 190 °C *in vacuo*.

Interaction between the deClMAn–ACH and Substrates Similarly to monomeric MAn, the possibility of the formation of CT complex between the deClMAn–ACH with solutes was studied using spectrophotometric measurement. Figure 4 shows the absorption spectra of acetone (1) and the mixture of deClMAn–ACH and acetone (2 and 3). In the case of 2 and 3, the concentration of MAn moiety based on the deClMAn–ACH was kept constant and the concentration of acetone was changed. When the concentration of acetone was increased, a new absorption band indicating formation of a CT complex was observed (3). Despite the higher concentration of acetone applied to the ClMAn–ACH, the absorption band due to CT did not appear in the wavelength range studied. Therefore, the copolymer retaining the structure similar to MAn moiety seems to take part in the formation of the CT complex.

As formation of the CT complex between deClMAn–ACH and acetone was suggested, the formation constant value of the complex was determined by a spectrophotometric technique using the Benesi–Hildebrand equation[22] in Eq. 1.

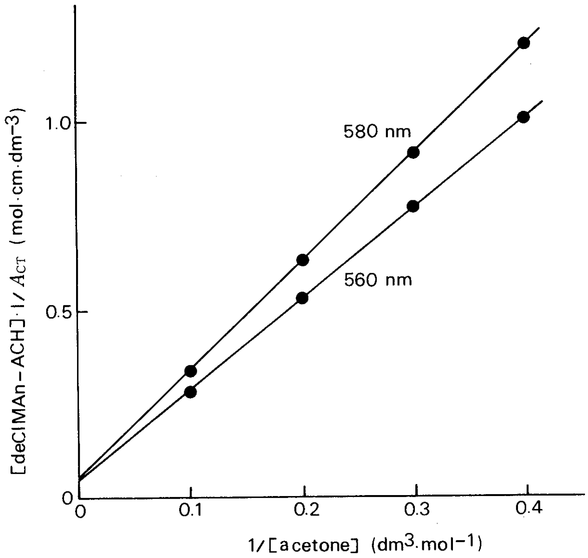

Fig. 5. Benesi–Hildebrand Plots of CT Absorption for deClMAn–ACH Copolymer–Acetone System in *n*-Hexane

[deClMAn–ACH] = 0.01 (mol·dm^{-3}).

Table II. Formation Constants, K_{CT}, of CT Complexes of Substrates with deClMAn–ACH and MAn in *n*-Hexane

Acceptor	Substrate	Temp. (°C)	K_{CT} (dm^3·mol^{-1})
deClMAn–ACH	Acetone	25	0.02
deClMAn–ACH	Methyl ethyl ketone	25	0.17
deClMAn–ACH	Methyl vinyl ketone	25	0.05
deClMAn–ACH	Tetrahydrofuran	25	0.00
MAn	Acetone	25	1.58[a]
MAn	Acetone	30	0.67[b]
MAn	Tetrahydrofuran	30	0.44[b]

a) Reference 24. *b*) Reference 4.

$$\frac{[\text{deClMAn}-\text{ACH}]\cdot l}{A_{CT}} = \frac{1}{\varepsilon_{CT}} + \frac{1}{K_{CT}\cdot\varepsilon_{CT}}\left(\frac{1}{[\text{B}]}\right) \qquad (1)$$

where [deClMAn–ACH] and [B] are the concentrations of MAn moiety based on the deClMAn–ACH and substrate, respectively, l is the optical cell length, and A_{CT} and ε_{CT} are absorption and molar absorption coefficient of the complex, respectively. This equation is applicable to the system under the conditions [B] ≫ [deClMAn–ACH]. Figure 5 shows the Benesi–Hildebrand plots for deClMAn–ACH and acetone at 560 and 580 nm. The figure shows that a straight line relation is completely satisfied at each wavelength and hence suggests that the composition of the complex formed between the copolymer and acetone is 1 : 1. Table II presents the formation constants of the complex determined by the Benesi–Hildebrand plot. The K_{CT} value determined for the deClMAn–ACH and acetone is lower than that for monomeric MAn and the substrate. The disturbance for the CT interaction between the polymer and the substrate is predominantly a result of steric hindrance in the polymer chains.[23] Thus, the decrease in the K_{CT} values in our study can also be assumed to be responsible for the steric hindrance.

In conclusion, ClMAn and ACH copolymerize in a ratio of 1 : 1, and the ClMAn–ACH copolymer is easily dehydrochlorinated to give deClMAn–ACH which has a structure similar to MAn. It is suggested that the deClMAn–ACH forms a weak CT complex with acetone where it works as a donor. As there are few polymers designed for an acceptor compared to those for a donor, the deClMAn–ACH is expected to be useful for a wide range of applications.

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