

Property of thermo-sensitive and redox-active poly(N-cyclopropylacrylamide-co-vinylferrocene) and poly(N-isopropylacrylamide-co-vinylferrocene)

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Thermo-sensitive and redox-active polymers were prepared by the copolymerisation of N-cyclopropyl (NCPAM) or N-isopropyl acrylamide (NIPAM) with varying content of vinyl ferrocene (VFc(II)). Aqueous solution of the copolymer showed LCST (lower critical solution temperature) depending on the ferrocene content in copolymers. LCST of the aqueous solution of these copolymers was decreased with increasing ferrocene content in the copolymers. The oxidation of ferrocene has led to a significant increase in LCST due to a transition from hydrophobic to hydrophilic property of ferrocene moiety in copolymers. The transition could be made reversibly by redox reaction using cerium sulfate as an oxidant and L-ascorbic acid as a reductant. Changes in the cloud point temperature accompanying the transition increased with increasing the amount of ferrocene in copolymer. © 1997 Elsevier Science Ltd.

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INTRODUCTION

The behavior of poly(N-substituted acrylamide)'s (PNAAm's) in aqueous solution is of quite some interest from both theoretical and practical perspectives¹. Some aqueous solutions of PNAAm's are known to be thermo-sensitive and phase separate or precipitate when the temperature rises to a lower critical solution temperature (LCST)².

Aqueous solutions of PNAAm are investigated to give a LCST and show thermoresponsive sensitivity depending on environmental temperature. These transitions have been exploited in the development of novel temperature sensitive methods for permeability control and protein phase separation. The LCST, and the accompanying change in polymer conformation, results from a balance between hydrogen-bonding and hydrophobic effects in aqueous solutions of PNAAm's. Its transition from a hydrophilic to a hydrophobic nature occurs rather abruptly at what is known as a LCST. Poly(N-isopropyl acrylamide) is a typical thermo-sensitive polymer, preparation, properties and uses have been summarised in a comprehensive review by Schild³.

On the other hand, Saji *et al.* reported^{4–9} the reversible formation and disruption of micelles by control of the redox state of the surfactant head group containing a ferrocenyl moiety. They prepared amphiphilic ferrocene derivatives which could form micelles including water-insoluble materials such as phthalocyanine dye. As the ferrocenyl moieties are oxidised, the ferrocene-containing surfactant micelles separate into monomers due to the enhancement in hydrophilicity of the surfactant head group. They also reported that such amphiphilic ferrocenyl compounds could

be changed reversibly to hydrophilic forms via electrochemical oxidation¹⁰. Surfactant-type ferrocenyl compounds formed micelles in the ferrous (II) state, which were disrupted into the ferric (III) state following electrochemical oxidation. They developed a new technique for electrochemical formation of an organic thin film by electrolysis of surfactants having ferrocenyl moieties (micelle disruption method)¹¹. This method is based on the controlled release of micelle-solubilised substances onto an electrode: the micelles are broken up into monomers when the ferrocenyl moiety is oxidised electrochemically. A solubilised material is then released from the micelles and deposited on the electrode.

Thermo-sensitive polymers can be rendered redox active through the introduction of a ferrocene moiety by copolymerisation of vinylferrocene. It is then possible to regulate the phase transition temperature of aqueous solution of such thermosensitive polymer by redox reactions. Therefore we prepared various poly(N-substituted acrylamide-co-vinylferrocene)s and demonstrated that the phase transition of aqueous solutions of the copolymer shifted to higher temperatures upon oxidation of the ferrocene moiety^{12,13}. We have demonstrated that oxidation of ferrocene-containing copolymer leads to a significant increase in LCST with increasing ferrocene content in copolymer. In this paper we prepared two other kinds of thermo-sensitive and redox-active copolyamides by the copolymerisation of vinylferrocene and two kinds of NAAMs. Thermo-sensitive properties of the copolymers were investigated in relation to the structure and hydrophilic and hydrophobic properties of the copolyamides. For the preparation of redox-active polyacrylamide, we prepared thermo-sensitive and redox-active copolymers

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containing VFc(II) as redox-active component, and N-cyclopropyl (NCPAM) or N-isopropyl acrylamide (NIPAM) as thermo-sensitive component. The synthesis and characterisation of thermo-sensitive polymers functionalised with redox-active groups and the influence of the redox-active groups in the reduced and oxidised state on the LCST transitions were described.

EXPERIMENTAL SECTION

Materials

Vinylferrocene (VFc(II)) was purchased from Aldrich and used without further purification. NCPAM was prepared by the reaction of cyclopropylamine with acryloyl chloride in the presence of triethylamine at 0°C. Crude product was recrystallised four times from benzene and n-hexane. Yield: 33.5%, m.p. = 40.0°C, IR: 1540 cm⁻¹, 1670 cm⁻¹ (-CO-NH-). ¹H-n.m.r. (CDCl₃): δ 7.8 ppm (NH), δ 6.2 ppm (CH₂=C), δ 5.6 ppm (-CH=C), δ 2.8 ppm (-N-CH-), δ 0.7 ppm (-CH₂-CH₂-).

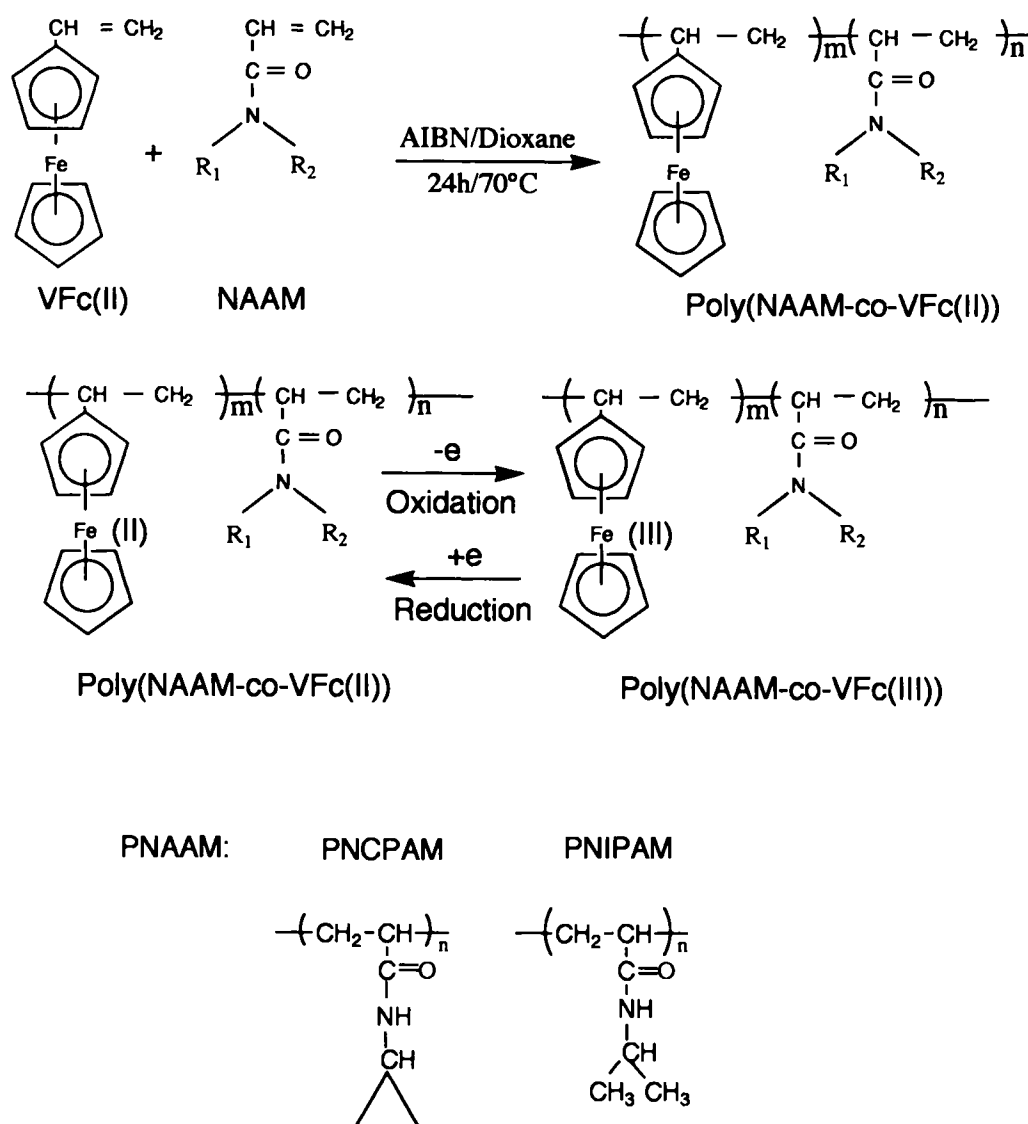
NIPAM was obtained from Kojin Chemical Co, Ltd and purified by recrystallisation twice from benzene and n-hexane. 2,2'-azobisisobutyronitrile (AIBN) was obtained from Tokyo Kasei Co, Ltd.

Polymerisation

P(NCPAM-co-VFc(II))s and P(NIPAM-co-VFc(II))s and homopolymers were prepared by a conventional radical polymerisation in dioxane with AIBN as an initiator. The appropriate amount of NCPAM or NIPAM and VFc(II) was dissolved in dioxane. Then the mixed solution was degassed by three alternate freeze-thaw cycles. After degassing, the tubes were placed in constant temperature baths controlled to 70°C. After a certain period of time, the reaction mixture was added dropwise to rapidly stirring diethyl ether to precipitate the copolymer. Precipitated copolymer was washed with diethyl ether and reprecipitated in this manner two more times. Precipitated product was then dried under vacuum and weighed.

Characterisation

The copolymer was oxidised with excess amount of Ce(SO₄)₂ and the composition was determined by the absorption spectra observed at 619 nm assigned to the ferric iron (e = 360) state¹⁴. Oxidation and reduction of the copolymers was carried out with equimolar amount of Ce(SO₄)₂ and L-ascorbic acid, respectively to the content of ferrocene moiety in copolymer. Cloud points of aqueous copolymer solutions (1 g/dl) were determined by the 50%



Scheme 1

Table 1 Copolymerization of (N-alkylsubstituted acrylamide)s with VFc(II)^a

Copolymer (mol. ratio)	Monomer (mmol)		Product (g)	Yield (%)	VFc(II) content ^b (mol%)	Molecular weight	
						$\overline{M}_w \times 10^{-4c}$	$\overline{M}_w/\overline{M}_n$
Poly(NCPAM-co-VFc(II))	NCPAM	VFc(II)					
(100:0)	10.3	0.0	9.9	99.7	0.0	21.1	4.41
(99:1)	10.3	0.104	0.87	84.5	0.65	1.62	8.21
(97:3)	10.3	0.319	1.10	97.8	1.99	7.4	2.32
Poly(NIPAM-co-VFc(II))	NIPAM	VFc(II)					
(100:0)	19.4	0.0	2.07	94.0	0.0	21.1	2.67
(99:1)	19.4	0.196	1.58	70.4	0.84	16.3	1.82
(97:3)	19.4	0.601	2.27	97.5	2.39	11.2	1.68

^aInitiator, AIBN 2 wt% to monomers; time, 24 hr; temperature, 70°C; solvent, dioxane; total monomer concentration, 4 mol/l^bCalculated from absorbance at 619 nm after oxidation^c \overline{M}_w was measured by GPC in DMF using a standard polystyrene as a reference

transparency level at 750 nm. UV spectra were recorded on a Shimadzu UV 210-A spectrophotometer. Molecular weights of copolymers were determined with Toyo Soda High Performance Gel Permeation Chromatography in N,N-dimethylformamide and standard polystyrene for calibration.

RESULTS AND DISCUSSION

Copolymerisations of VFc(II) with NCPAM or NIPAM were carried out using conventional radical polymerisation. Scheme 1 shows the procedure of preparation and redox reaction for thermo-sensitive and redox-active poly(N-substituted acrylamide-co-vinyl ferrocene) (poly(NAAm-co-VFc(II))), that is poly(NCPAM-co-VFc(II)) and poly(NIPAM-co-VFc(II)). In order to introduce a reversible property in the polyacrylamide network, the redox process ferrocene(II)/ferrocenium(III) must be chemically reversible. Table 1 shows the results of copolymerisation reaction and the characterisation of poly(NAAm-co-VFc(II))s. Polymerisation of vinylferrocene is known to be difficult because the ferrocenium ion(II) plays as a radical scavenger in the polymerisation system. Therefore copolymerisation of VFc(II) with N-substituted acrylamide resulted in the retardation of polymerisation rate according to the ferrocene content in monomers. The molecular weights of resultant copolymers were also decreased with increasing ferrocene content in monomer. The decrease in molecular weight demonstrated that ferrocene moiety played a radical scavenger in the copolymerisation system. On the other hand, polymerisability of N-substituted acrylamides were generally high in comparison with that of VFc(II). Although the molecular weights of copolymerisation were relatively low, copolymerisation was proceeded to give a large amount of copolymers. Four kinds of copolymers with different ferrocene content were obtained copolymerising three different monomer ratios of VFc(II) and NCPAM or NIPAM which are 0/100, 1/99 and 3/97.

The ferrocene content in poly(NAAm-co-VFc(II))s is always less than ferrocene content in monomer^{12,13}. Ferrocene content in copolymer was determined by the absorption of oxidised ferrocene moiety in copolymer observed at 619 nm in an aqueous solution. The value of ferrocene content derived from the spectroscopy is smaller than the monomer ratio used in copolymerisation. The molecular weight distribution of poly(NAAm-co-VFc(II))s

were determined by gel permeation chromatography using standard polystyrene as a reference. Homopolymer had a large molecular weight and relatively broader molecular weight distribution. The molecular weight was decreased with increasing ferrocene content in monomer ratio. The molecular weight distribution became narrower with increasing VFc(II) content in monomer ratio. These results show that retardation of copolymerisation is presumably due to extensive chain transfer involving growing chain ends and VFc(II) molecules. The polymerisation of VFc(II) was studied extensively and the kinetics of radical polymerisation of VFc(II) also investigated. The term 'intraelectron' termination is a general characteristic of radical polymerisation of VFc(II)¹⁵. George *et al.*, have shown that organic solutions of ferrocenium cations decompose to give iron(III) compounds, and hence it seems that after the initial electron transfer which terminates the polymer chain, the cation immediately undergoes further reaction to give iron(III) species^{16,17}. Furthermore, the resultant odd electron species are inactive in further polymerisation reactions. The lower molecular weights are due to the specific 'intraelectron' termination of VFc(II).

All of the copolymers showed the same solubility as the homopolymers and were soluble in various solvents such as water. Previous studies indicated that ferrocene(II) was converted to ferricium iron(III) state when treated with

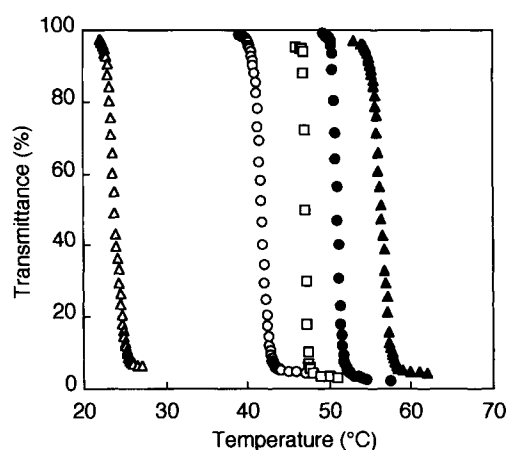


Figure 1 Effect of temperature on transmittance of aqueous copolymer solutions before and after oxidation. □: PNCAM; ○: poly(NCPAM-co-VFc(II))(99:1); ●: ox-poly(NCPAM-co-VFc(II))(99:1); △: poly(NCPAM-co-VFc(II))(97:3); ▲: ox-poly(NCPAM-co-VFc(II))(97:3)

$\text{Ce}(\text{SO}_4)_2$ in aqueous solution and reversed to ferrocenyl iron(II) state when treated with L-ascorbic acid¹². Therefore the copolymers containing ferrocene(II) were oxidised and reduced repeatedly with simple chemical treatment. The characteristic property of the copolymer was also converted to hydrophilic when treated with $\text{Ce}(\text{SO}_4)_2$ as oxidant and reversed to hydrophobic when treated with L-ascorbic acid as reductant. These changes could be repeated reversibly by redox reaction.

The phase transition behavior of copolymer was evaluated by measuring optical transmittance of the copolymer solutions at 750 nm as a function of temperature in a Shimadzu UV-210A spectrophotometer fitted with temperature controller. Figure 1 shows a plot of reduced transmittance versus temperature of PNCPAM and three different kinds of poly(NCPAM-co-VFc(II))s solutions before and after oxidation (ox-poly(NCPAM-co-VFc(II))). The cloud point temperatures of the solution prepared from poly(NCPAM-co-VFc(II))s are quite reproducible. Transmittance of copolymer solution changed sharply with temperature at various ferrocene contents in copolymer. All the changes of the transmittance occurred sharply within 2–3°C for the homopolymer and the copolymers.

In Figure 2, the LCST of copolymers are shown as a function of VFc(II) content for poly(NCPAM-co-VFc(II))s. The change in LCST was found to be proportional to the VFc(II) content in copolymers. The oxidation of these poly(NCPAM-co-VFc(II))s treated with $\text{Ce}(\text{SO}_4)_2$ leads to a significant increase of LCST of copolymers. PNCPAM showed a relatively high LCST throughout a wide concentration range. Thermo-sensitivity of aqueous copolymer solution containing ferrocene moiety indicates that copolymer was more hydrophobic than original PNCPAM. Poly(NCPAM-co-VFc(II))s changed its hydrophobic property with temperature and precipitated above LCST. LCST of copolymer was found to decrease extremely with increasing content of ferrocene in copolymer. The significant shifts of LCST of the copolymer solution were observed due to the transformation from hydrophobic to hydrophilic characteristics of ferrocenyl ring even at lower ferrocene content (0.65%). Transmittance of copolymer solution changed sharply with temperature even at higher ferrocene content in copolymer.

Saji *et al.* reported^{9,10} that surfactant-type ferrocenyl compound formed micelle in the ferrocenyl(II) state and disrupted in the ferric(III) state with electrochemical

oxidation. Ferrocenyl(II) iron in copolymer was oxidised smoothly to result in ferric(III) iron which provides the hydrophilic property in copolymer. Such redox chemical change of the hydrophobic–hydrophilic property of the copolymer with oxidation and reduction could be repeated reversibly.

Figure 3 also shows the effect of temperature on the transmittance of aqueous PNIPAM and poly(NIPAM-co-VFc(II))s solutions before and after oxidation (ox-poly(NIPAM-co-VFc(II))). PNIPAM showed a LCST at 33.3°C which is more hydrophobic than PNCPAM due to the introduction of methyl group into N-amide group. PNIPAM changed its hydrophobic property with temperature and precipitated above LCST. The introduction of ferrocene moiety into PNIPAM leads to a little decrease of LCST of PNIPAM. The LCSTs of poly(NIPAM-co-VFc(II))s are shown as a function of VFc(II) content in poly(NIPAM-co-VFc(II))s (Figure 4). The LCST was decreased gradually with increasing the VFc(II) content in copolymers. The oxidation of these poly(NIPAM-co-VFc(II))s treated with $\text{Ce}(\text{SO}_4)_2$ leads to a little increase of LCST of copolymers. These changes are not so significant in comparison with those of poly(NCPAM-co-VFc(II))s. The copolymer was more hydrophobic than original PNIPAM and the shifts of LCST of the copolymer

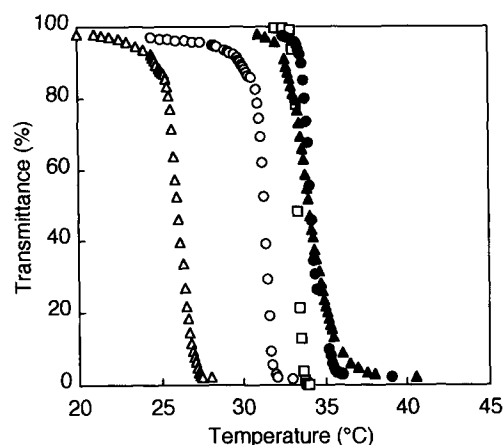


Figure 3 Effect of temperature on transmittance of aqueous copolymer solutions before and after oxidation. □: PNIPAM; ○: poly(NIPAM-co-VFc(II))(99:1); ●: ox-poly(NIPAM-co-VFc(II))(99:1); △: poly(NIPAM-co-VFc(II))(97:3); ▲: ox-poly(NIPAM-co-VFc(II))(97:3)

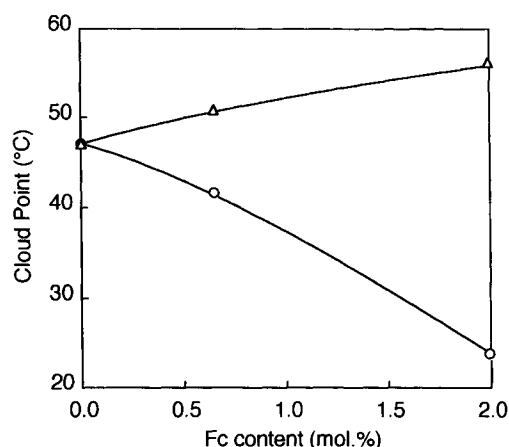


Figure 2 Dependence of the cloud point temperature on the ferrocene content for poly(NCPAM-co-VFc(II)) before (○) and after (△) oxidation

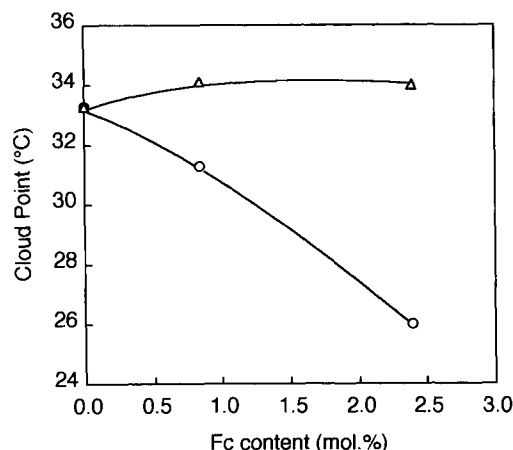


Figure 4 Dependence of the cloud point temperature on the ferrocene content for poly(NIPAM-co-VFc(II)) before (○) and after (△) oxidation

Table 2 Cloud points of poly(N-alkylsubstituted acrylamide)s and poly(N-alkylsubstituted acrylamide-co-VFc(II)s

Polymer (mol. ratio)	Cloud point		
	red. (°C)	ox. (°C)	Δ (ox. - red.) (°C)
Poly(NCPAM-co-VFc(II))			
(100:0)	47.1	—	
(99:1)	41.7	51.0	9.3
(97:3)	23.8	56.3	32.5
Poly(NIPAM-co-VFc(II))			
(100:0)	33.3	—	
(99:1)	31.3	34.1	2.8
(97:3)	26.0	34.0	8.0

Concentration of polymer = 1.0 g/l

solution were slightly observed due to the little influence of transformation from hydrophobic to hydrophilic characteristics of the copolymers.

Table 2 summarised the cloud points of copolymers with and without VFc(II) and before and after oxidation. Introduction of VFc(II) into PNAAMs leads to a significant decrease of cloud point. This effect of introduction of VFc(II) into polymer chain is significant with more hydrophobic polyamides like PNCPAM. In case of PNCPAM, introduction of 1.99% VFc(II) into PNCPAM leads to a significant shift of cloud point between 56.3 and 23.8°C. Phase separation as evidenced by the drastic reduction in the transmittance occurred at about LCST of 47.1°C for PNCPAM, 41.7°C for poly(NCPAM-co-VFc(II)) (99:1) and 23.8°C for poly(NCPAM-co-VFc(II)) (97:3). However, in case of more hydrophobic polymers such as PNIPAM, introduction of VFc(II) leads to little effect on cloud point.

The behavior of a polymer in a given medium reflects the balance of like and unlike interactions among its own segments and the surrounding molecules. In the case of aqueous solutions, the solvent-solvent interaction is particularly strong as indicated by its partially ordered structure. Ordering the structure of solutes such as PNAAM in aqueous solution results from specific orientations requiring the formation of a hydrogen-bond with the already arranged water molecules. This becomes especially important when water molecules must reorient around non-polar regions of solutes, being unable to where hydrogen bonds are formed between the polymer polar groups and water molecules which is the initial driving force for dissolution temperature. If the concentration of the polymer is high enough, this replacement of polymer-water contacts with polymer-polymer and water-water contacts is manifested by precipitation.

Introduction of ferrocenyl moiety into thermo-sensitive hydrophilic PNAAMs leads to the large shift of LCST of polymer to the lower temperature due to the addition of hydrophobic property of ferrocene moiety. Furthermore, oxidation of ferrocene-containing thermo-sensitive poly (NAAm-co-VFc(II)s leads to a significant shift of LCST of copolymers to a higher temperature depending on the addition of the hydrophilic property of ferricinium ion(III) state of ferrocene ring. The content of VFc(II) in copolymers increases with increasing the hydrophobic property and decreasing the cloud point temperature. Furthermore difference between cloud points before and after oxidation was large with the ferrocene content in copolymers. These results mean that hydrophobic property of VFc(II) moiety added to the PNAAM hydrophilic main chain. Oxidation of ferrocenyl moiety leads to copolymers becoming more hydrophilic and an increase in cloud point temperature. The hydrophobic and hydrophilic change of thermo-sensitive property of these copolymers in aqueous solution in accordance with oxidation and reduction was reversible. The copolymer was oxidised to be more hydrophilic and reduced to be more hydrophobic nature in aqueous solution. These properties provided the reversible change of cloud point of the copolymer solution with oxidation and reduction.

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