Institute for Polymer Research
27th Annual Symposium

Symposium documents for

Rodolfo Salgado

Abstract

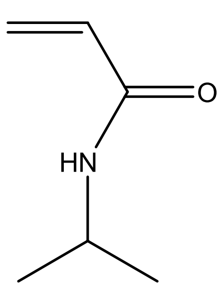
Presentation

Poster

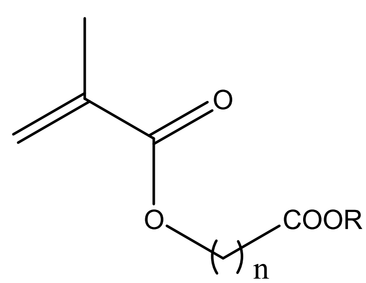
“New temperature- and pH-sensitive smart polymers containing methacrylic derivatives with hydrophobic spacers”

Rodolfo Salgado-Rodríguez, Angel Licea-Claveríe
Centro de Graduados e Investigación, Instituto Tecnológico de Tijuana, A.P.1166
22000 Tijuana, B.C.; MEXICO

This work deals with temperature- and pH-sensitive materials, which have many potential applications, e.g. in controlled release of drugs or in separation processes of dissolved molecules.[1] The research was focused on the synthesis and characterization of linear and crosslinked polymers containing *N*-isopropylacrylamide[2,3] (NIPAAm) (**I**) and new methacrylic acid-derivative monomers (**II**). These monomers have as distinctive feature a methylene chain as spacer, which varies in their length (4, 7 and 10 methylene units). The effect of the length of methylene spacer and the effect of the presence of carboxylic acid groups on phase transition temperatures, and swelling capability of the produced materials were studied as a function of temperature and pH.[4]



I



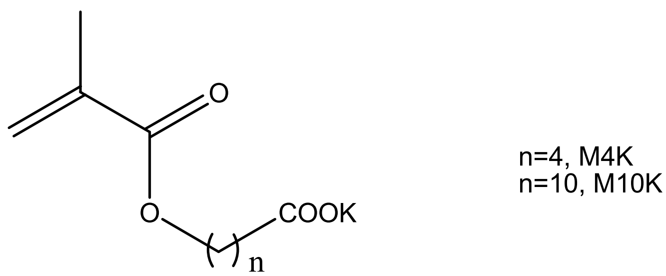
II

For R=CH_3
n=4, MOP4
n=7, MOP7
n=10, MOP10

For R=H
n=4, MOD4
n=7, MOD7
n=10, MOD10

Starting from monomers with methylesther end-group, MOP4, MOP7 and MOP10, copolymers containing NIPAAm in different amounts were synthesized. Their solution behavior showed that their LCST (referred to PNIPAAm) was lower when the hydrophobic comonomer content was increased. On the other hand, copolymers containing NIPAAm were also prepared, starting from monomers containing a carboxylic acid group, MOD4, MOD7 and MOD10. Studies in aqueous solution of all copolymers were performed in deionized water and buffer solutions at different pH values. Upon incorporation of the ionizable COOH group the range of values of LCST became wider.

Homopolymeric and copolymeric gels containing NIPAAm were prepared, starting from monomers in the form a potassium salt (M4K and M10K) (**III**). The swelling behavior was studied varying the temperature and using solutions with different pH values (Figure 1).



III

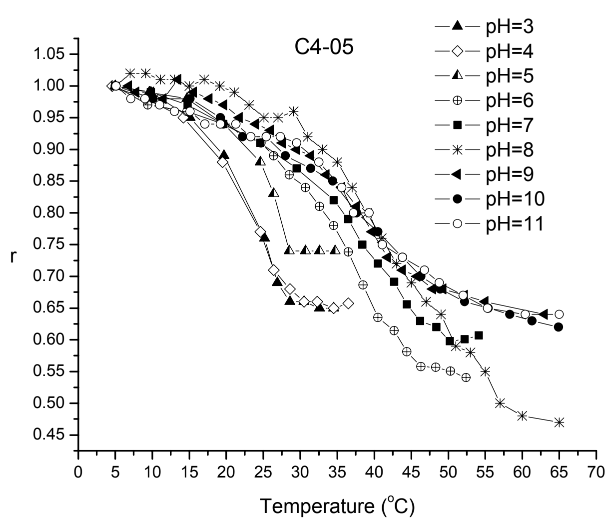


Figure 1. Temperature and pH dependence of the swelling ratio (r) for C4-05 (gel containing NIPAAm : M4K, 95:5, mol)

Phase transition temperatures (T_c) ranging from 14 to 64°C were obtained (Table 1). The effect of the pH of the swelling medium was essential to change the T_c and the amount of solution retained by the gels. Above T_c, the hydrophobic interaction becomes dominant, causing polymer to collapse and phase separate and expel water.[5] The difference in the functional group of the comonomers used in the linear copolymers (free acid) and copolymeric gels (potassium salt) caused that the phase transition temperatures were not fully comparable. However, with pH values above 7 there are strong similarities in the behavior of these materials.

Table 1. Phase transition temperature (T_c) depending on pH

	T_c (°C)									
GELS	**DI Water**	**pH=3**	**pH=4**	**pH=5**	**pH=6**	**pH=7**	**pH=8**	**pH=9**	**pH=10**	**pH=11**
CN	33	----	----	----	----	----	----	----	----	----
C4-05	30	26	25	27	40	41	50	41	45	43
C4-10	37	19	20	24	53	48	53	47	53	50
C4-15	51	17	18	21	57	57	57	52	50	56
C4-20	N	14	17	18	64	N	N	N	N	N
C10-05	28	26	25	24	26	31	35	33	34	36
C10-10	25	21	21	22	28	32	38	37	38	41
C10-15	36	19	20	21	29	34	41	45	47	46
C10-20	29	N	N	N	24	33	44	49	49	53

ACKNOWLEDGEMENT

R. Salgado-Rodríguez thanks DAAD-Germany for financing his PhD-Sandwich program.

We are grateful to CONACYT-México (Project Nr. 28022-U) and Volkswagen Foundation-Germany (Project Nr. I/76 065) for financial support of this work.

We thank specially for valuable technical support I. Rivero (NMR), D. Scheller (NMR), I. Poitz (DSC) and C. Meissner (SLS).

REFERENCES

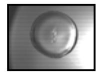
1. Hoffman, A. S.; *Macromol. Symp*., **1995**, *98*, 645.
2. Heskins, M.; Guillet, J. E.; *J.Macromol.Sci.Chem.*, **1968**, *A2*, 1441.
3. Schild, H. G.; *Progress in Polymer Science*, **1992**, *17*, 163.
4. Salgado-Rodríguez, R.; Licea-Claveríe, A.; Arndt, K. F. *European Polymer Journal* **2004**, *40*, 1931.
5. Feil, H.; Bae, Y. H.; Feijen, J.; Kim, S. W.; Macromolecules, **1993**, *26*, 2496.

1

INSTITUTO TECNOLÓGICO DE TIJUANA

CENTRO DE GRADUADOS E INVESTIGACIÓN EN QUÍMICA

“New temperature- and pH-sensitive smart polymers containing methacrylic derivatives with hydrophobic spacers”



DR. RODOLFO SALGADO RODRÍGUEZ

DR. ANGEL LICEA CLAVERÍE

2

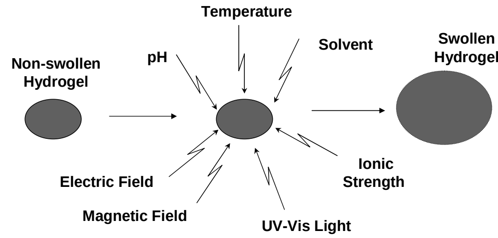
- **INTRODUCTION**
- **GELS**
- **CONCLUSIONS**

3

INTRODUCTION

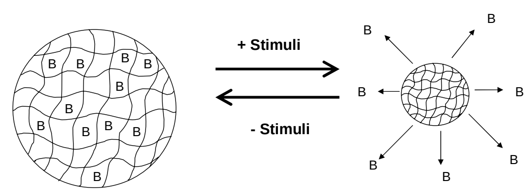
4

“Smart” Gels



5

Controlled Drug Delivery

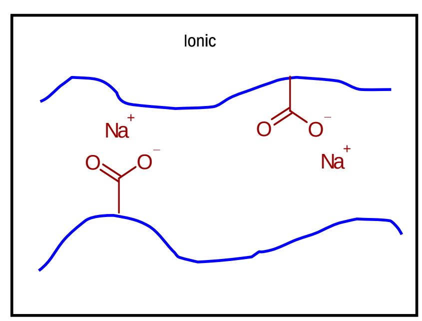


B = Drug molecule

6

Fundamental Interactions

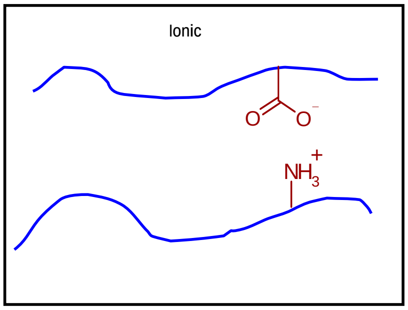
Repulsion



7

Fundamental Interactions

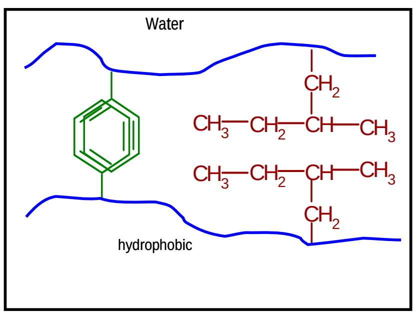
Attractions



8

Fundamental Interactions

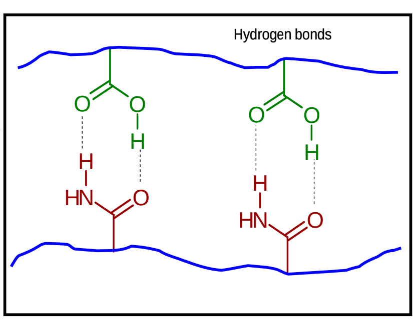
Attractions



9

Fundamental Interactions

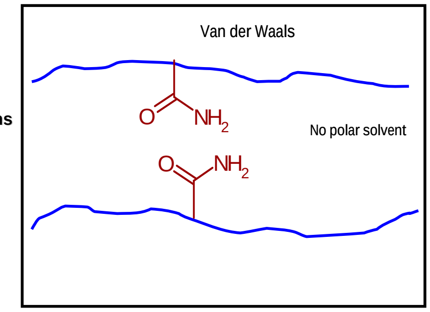
Attractions



10

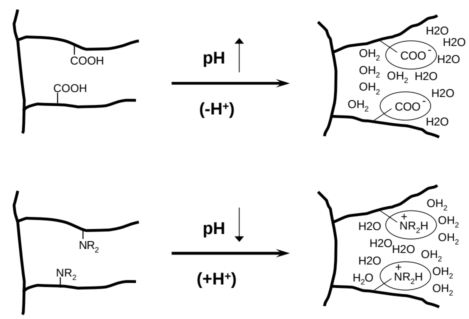
Fundamental Interactions

Attractions



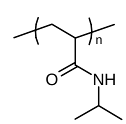
11

pH-sensitive



12

Poli (*N*-isopropylacrylamide) PNIPAAm

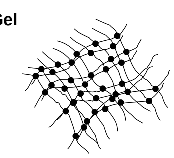


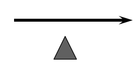
Lineal Polymer

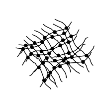
Lower Critical Solution Temperature (LCST)

T = 32ºC

NIPAAm-Gel

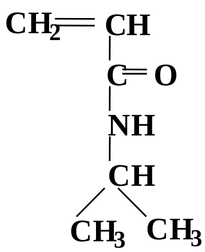




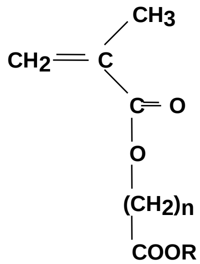


T < 32ºC **T > 32ºC**

13



NIPAAm



n= 4 and 10

R= CH_3 , **H**

14

G E L S

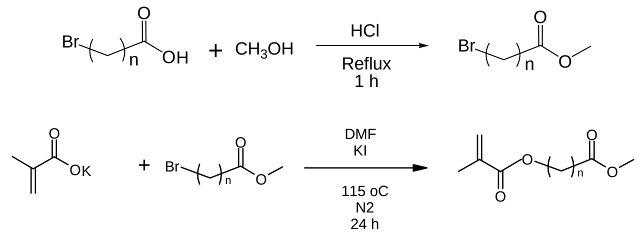
15

OBJECTIVE

SYNTHESIS AND CHARACTERIZATION OF COPOLYMERIC GELS SENSITIVE TO TEMPERATURE AND pH CONTAINING *N*-ISOPROPYLACRYLAMIDE AND MONOMERIC DERIVATIVES FROM METHACRYLIC ACID WITH HYDROPHOBIC SPACERS.

16

Synthesis of protected monomers

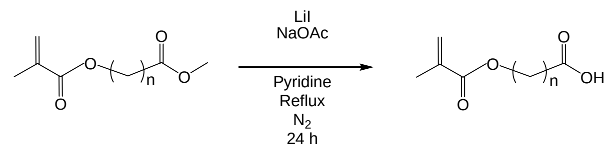


n = 4 ⇨ MOP4

n = 10 ⇨ MOP10

17

Synthesis of deprotected monomers

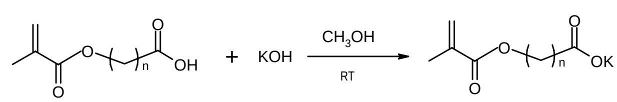


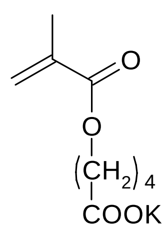
n = 4 ⇨ MOD4

n = 10 ⇨ MOD10

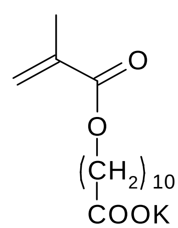
18

Synthesis of monomers as potassium salts



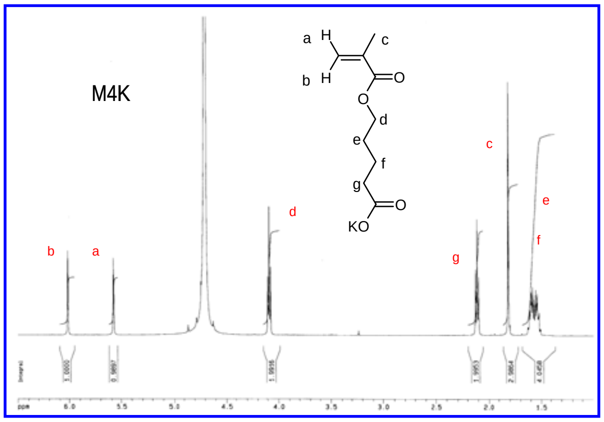


M4K



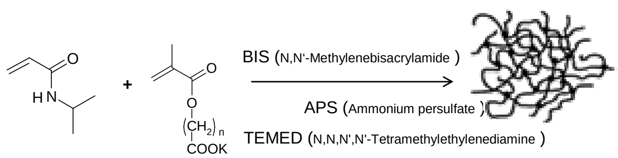
M10K

19



20

PREPARATION OF COPOLYMERIC GELS



NIPAAm

(M4K and M10K)

5,10, 15 and 20 % mol

Deionized Water

21

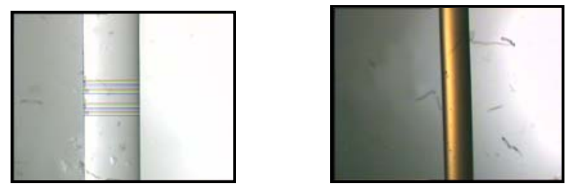
Gels prepared in glass capillary tubes and between glass plates

Molar composition	C	P
100% NIPAAm	CN	PN
100% M4K	C4	P4
100% M10K	C10	P10
5% mol M4K	C4-05	P4-05
10% mol M4K	C4-10	P4-10
15% mol M4K	C4-15	P4-15
20% mol M4K	C4-20	P4-20
5% mol M10K	C10-05	P10-05
10% mol M10K	C10-10	P10-10
15% mol M10K	C10-15	P10-15
20% mol M10K	C10-20	P10-20

22

Gels prepared in glass capillary tubes (Gels C)

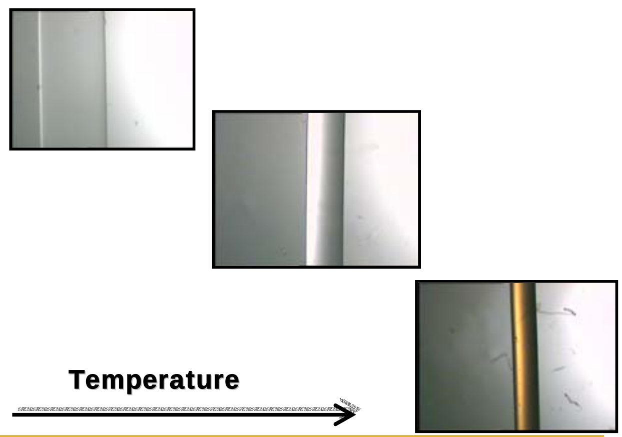
- Open capillary tubes (both sides) of 100 x 1.0 mmØ
- Essays tubes of 100 x 16 mmØ
- Gels rinsed with deionized water
- Gels equilibrated in deionized water and in buffer solutions of pH= 3,4,5,6,7,8,9,10 and 11
- Measurement of diameter of gels at certain temperatures
- Heating of gels starting from 5 ºC



$r = d/d_0$

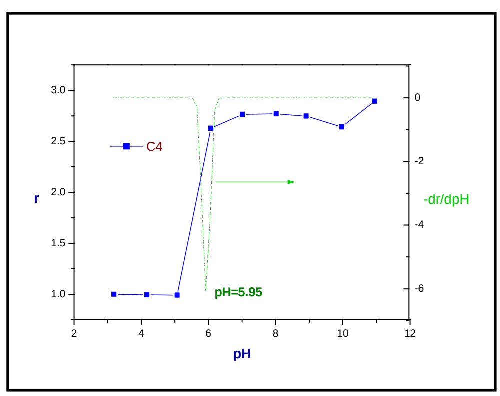
d_0 initial diameter
d diameter at temperature T

23



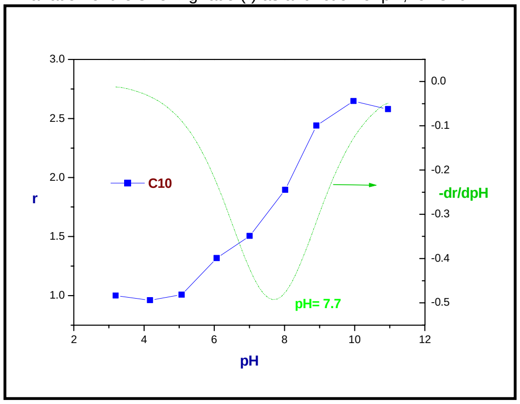
24

Variation of the swelling ratio (r) as a function of pH, for C4



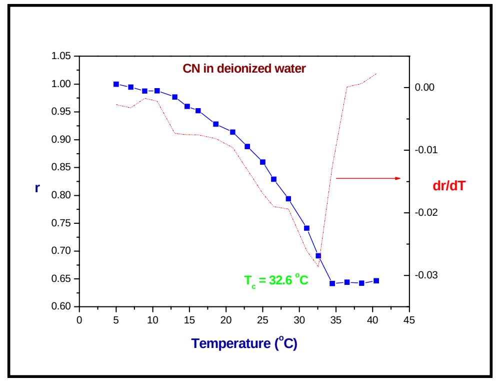
25

Variation of the swelling ratio (r) as a function of pH, for C10



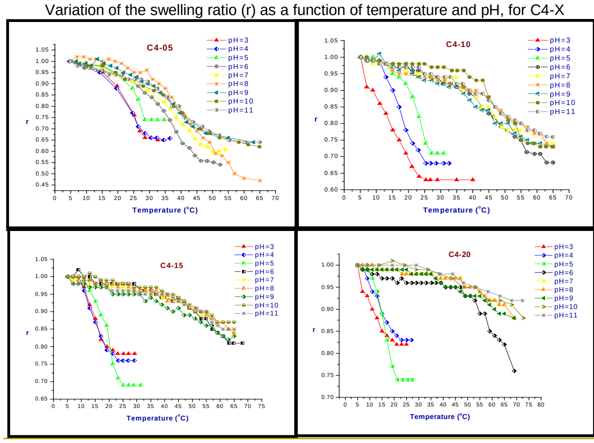
28

Critical temperature for CN



26

Variation of the swelling ratio (r) as a function of temperature and pH, for C4-X



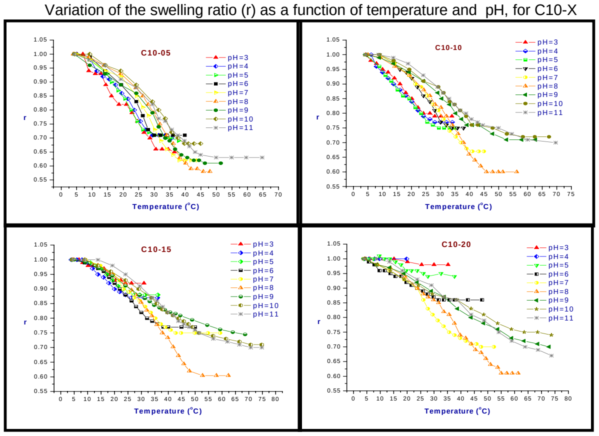
29

Critical temperature for the copolymeric gels

GELS	Water DI	pH=3	pH=4	pH=5	pH=6	pH=7	pH=8	pH=9	pH=10	pH=11
		Critical temperature (°C)								
CN	33	----	----	----	----	----	----	----	----	----
C4-05	30	26	25	27	40	41	50	41	45	43
C4-10	37	19	20	24	53	48	53	47	53	50
C4-15	51	17	18	21	57	57	57	52	50	56
C4-20	N	14	17	18	64	N	N	N	N	N
C10-05	28	26	25	24	26	31	35	33	34	36
C10-10	25	21	21	22	28	32	38	37	38	41
C10-15	36	19	20	21	29	34	41	45	47	46
C10-20	29	N	N	N	24	33	44	49	49	53

27

Variation of the swelling ratio (r) as a function of temperature and pH, for C10-X



30

Gels prepared between glass plates (Gels P)

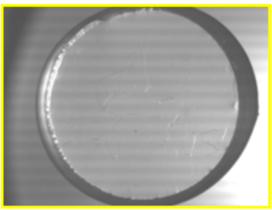
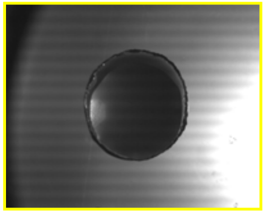
-Discs equilibrated in deionized water and in buffer solutions (pH 3 – 11)
-Equilibrium-swelling at temperatures of: 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 °C.

$$Q = \frac{W_h - W_x}{W_x}$$

where:
Q = Equilibrium swelling ratio
W_h= Weight of the swollen gel
W_x= Weight of the dry gel

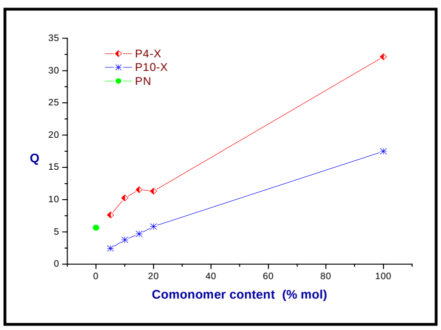
31



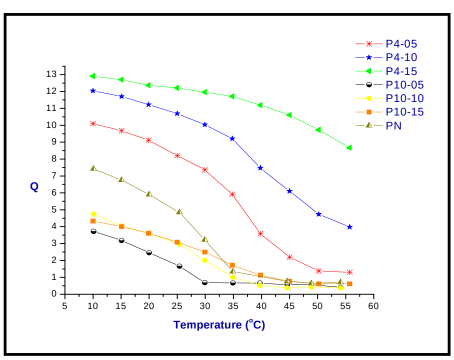
32

Variation of the equilibrium swelling ratio (Q) as a function of the comonomer content at room temperature for gels prepared between glass plates



33

Effect of the temperature and composition of the gel in the swelling ratio in deionized water



34

CONCLUSIONS

- Two new monomeric derivatives from methacrylic acid with free acid groups differing only in the spacer (chain of methylenes with n = 4 and 10), were prepared.
- Copolymeric gels of NIPAAm with M4K and M10K were prepared successfully and they were pH- and temperature sensitive as well. The critical temperatures values obtained for these materials ranged from 14 to 64ºC .
- An hydrophobic effect due to the mehtylene spacer chains was observed: A higher swelling ratio for the gels containing M4K compared to M10K.
- The series of gels with M4K show a bigger swelling change at pH=5 while the gels with M10K show this change at pH=8, those values are close to the critical pH of parent homopolymers.

35

CONCLUSIONS

- The geometrical shape of the gels affects the swelling behavior: thin cylinders show more defined phase transition temperatures than discs that deswell over a wider temperature range.
- In agreement with the results obtained in this work, it is possible to design a polymeric material with an specific phase transition temperature at a certain pH using a different type and content of comonomer.
- Several materials prepared in this work could be excellent candidates for applications in controlled drug delivery as a function of pH and/or temperature changes.

36

Acknowledgements

- Dr. Angel Licea Claverie
- Profr. Dr. Karl Friedrich Arndt
- CONACyT-Mexico
- DAAD-Germany
- Volkswagen Foundation- Germany
- Thanks specially for valuable technical support to : I. Rivero (NMR), D. Scheller (NMR), I. Poitz (DSC) and C. Meissner (SLS).

CONACYT
Consejo Nacional de Ciencia y Tecnología

Foundation

DAAD Deutscher Akademischer Austausch Dienst German Academic Exchange Service

pH-tunable temperature sensitive materials from NIPAAm-methacrylic acid copolymers with hydrophobic spacers

R. Salgado-Rodríguez[1], **A. Licea-Claveríe**[1] **and K.F. Arndt**[2]

1.-Centro de Graduados e Investigación, Instituto Tecnológico de Tijuana, A.P.1166-22000 Tijuana, B.C., MEXICO

2.-Institut für Physikalische Chemie und Elektrochemie, Technische Universität Dresden, D-01062 Dresden, GERMANY

Goal

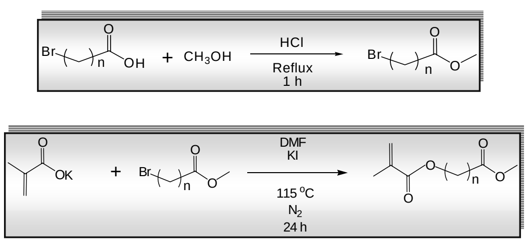
The aim of this work was to develop a series of NIPAAm-copolymers with tuning capacity for their LCST based on comonomers with hydrophobic spacers and hydrophilic ionizable groups. Furthermore, the study of the importance of intrachain hydrogen-bonding, regarding LCST of NIPAAm copolymers in pure water and in solutions with varying pH using partially hydrophobic comonomers is a further goal of this work. Finally, since linear copolymers can be easily characterized, their investigation is the basis for the better understanding of the behaviour of their corresponding polymer networks to be developed in the future.

Introduction

During the last years there has been a growing interest in temperature-sensitive polymers because they are potential candidates for applications as intelligent sensors, separation systems and drug release devices. It has been shown that the temperature-sensitivity of these polymers is connected with their lower critical solution temperature (LCST). There are some polymers which exhibit a LCST in aqueous solutions, the most studied polymer being the poly (***N***-isopropylacrylamide) (PNIPAAm) whose LCST lies between 30 and 35 ºC . The LCST of these polymers is a result of a fine balance of hydrophilic and hydrophobic groups in their molecular structure. If the balance is slightly altered there is a possibility to vary its LCST. This can be achieved by varying the chemical composition of the polymer.

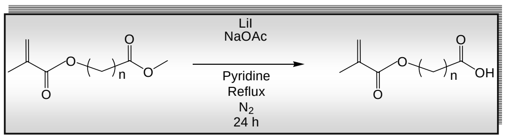
Experimental

Synthesis of hydrophobic monomer derived from methacrylic acid:



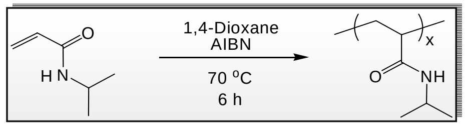
n = 4, 7 and 10

Synthesis of hydrophilic monomer derived from methacrylic acid:

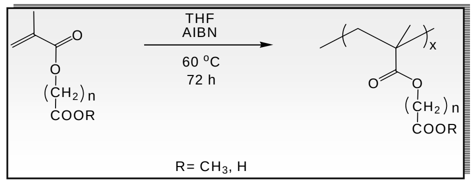


n = 4, 7 and 10

Synthesis of PNIPAAm via free radical polymerization

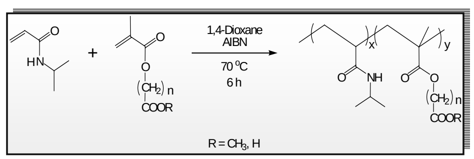


Synthesis of homopolymers



n = 4, 7 and 10

Synthesis of copolymers



n = 4, 7 and 10
y = 5, 10, 15, 20 and 25 mol%

Results

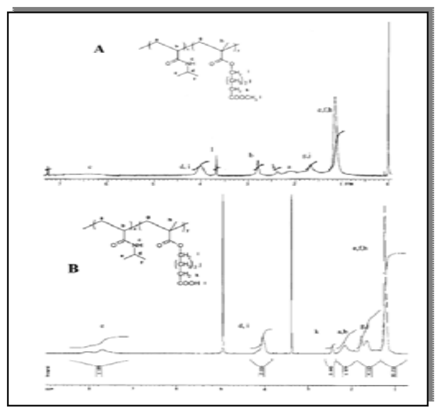


Figure 1. Selected NMR-spectra of NIPAAm-copolymers: (A) copolymers with protected acid groups, (B) copolymers with free acid groups.

Table 1. Results of protected copolymers characterization.

Polymer	Co-monomer content [mol%]	dn/dc [mL/g]	M_w [g/mol]	R_g in THF [nm]	T_g [ºC]	Yield [%]
PNIPAAm	-----	0.09299	237 000	27	139	92
COPN4-05	6.2	0.09530	264 000	27	128	77
COPN4-10	9.9	0.08870	292 000	28	114	87
COPN4-15	16.8	0.08900	281 000	27	106	82
COPN4-20	20.4	0.08380	297 000	24	106	85
COPN4-25	19.6	0.09330	208 000	21	97	84
COPN7-05	7.8	0.08098	398 000	31	128	90
COPN7-10	11.6	0.07264	514 000	31	114	87
COPN7-15	15.5	0.08871	406 000	34	105	70
COPN7-20	24.6	0.04360	832 000	32	104	78
COPN7-25	29.0	0.08207	445 000	33	93	73
COPN10-05	4.8	0.09141	368 000	32	127	81
COPN10-10	8.4	0.09105	343 000	30	108	73
COPN10-15	11.3	0.08514	414 000	44	100	45
COPN10-20	23.0	0.08613	296 000	30	78	89
COPN10-25	25.6	0.07859	332 000	32	68	98

Table 2. Results of deprotected copolymers characterization.

Polymer	Co-monomer content [%mol]	dn/dc [mL/g]	M_w [$gmol^{-1}$]	R_g in THF [nm]	T_g [ºC]	Yield [%]
CODN4-05	7.8	0.09310	291000	26	133.8	94.3
CODN4-10	12.4	0.09219	340000	23	126.7	82.0
CODN4-15	18.0	0.16656	241000	19*	121.8	87.0
CODN4-20	24	0.16912	310000	30*	117.1	95.0
CODN7-05	7.2	0.09438	354 000	29	127.9	90.9
CODN7-10	12.4	0.09497	318 000	24	118.6	86.0
CODN7-15	17.4	0.16564	275 000	19*	109.6	93.5
CODN10-05	6.6	0.09370	287 000	24	126.4	94.2
CODN10-10	12.8	0.09352	289 000	22	112.5	94.3
CODN10-15	17.3	0.17395	231 000	23*	99.7	90.3

Behaviour of linear polymer in aqueous solution

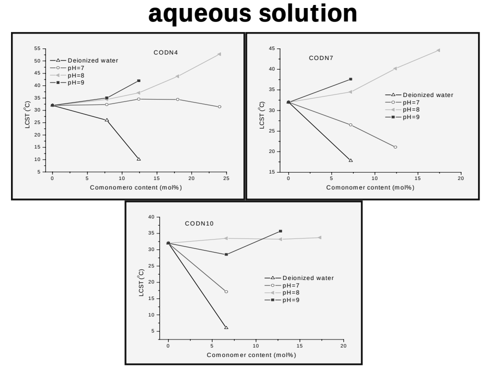


Figure 2. LCST behaviour of NIPAAm-copolymers with free acid groups in buffers of different pH as a function of comonomer content.

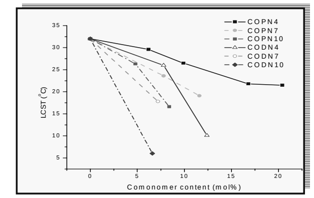


Figure 3. LCST behaviour of NIPAAm-copolymers in pure water in dependence on comonomer content.

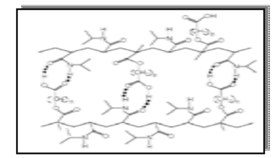


Figure 4. Proposed hydrogen-bonding interactions in the NIPAAm-copolymers.

Conclusions

- ☑ Two series of random NIPAAm-copolymers were successfully prepared using acid comonomers with aliphatic spacers (4, 7 and 10 methylene units) having the acid group either methoxy-protected or free.
- ☑ Solution free radical polymerization proved to be a good technique for their preparation since high yields (close to 90%) in 6 h were achieved. Furthermore, the copolymer composition was close to the monomer feed composition indicating a truly random distribution of the monomeric units in the copolymers.
- ☑ In the solid state, the aliphatic spacers bring side chain flexibility lowering the T_g of the copolymers while the free acid groups give the chance of interchain hydrogen-bonding increasing the T_g as a result.
- ☑ The water solubility and LCST behaviour of the prepared NIPAAm-copolymers depends on the hydrophilic/ hydrophobic balance in the copolymer chain and on the hydrogen-bonding capabilities from its chemical structure. The hydrophilic/hydrophobic balance depends mainly on three elements, (a) the amount of comonomer; (b) the kind of comonomer, regarding the spacer (n = 4, 7 and 10, methylene units) and the acid group (protected or free); (c) the pH of the solution of the copolymer, which affects the extent of ionization of the carboxylic acid groups.
- ☑ Finally, our results show that both: hydrophobic interactions and hydrogen- bonding are very important for the behaviour of NIPAAm-copolymers depending strongly on the fine chemical structure of the used copolymeric units.

Acknowledgements

- R. Salgado-Rodríguez thanks to DAAD-Germany for financing his PhD-exchange program.
- We gratefully acknowledges the financial support of CONACYT-México (Project Nr. 28022-U) and Volkswagen Foundation-Germany (Project Nr. I/76 065).
- We thank specially I. Rivero (NMR), D. Scheller (NMR), I. Poitz (DSC) and C. Meissner (SLS) for valuable technical support.