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ORIGINAL CONTRIBUTION

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Thermodynamics of the compression of poly(isobutyl cyanoacrylate) monolayers at acid, neutral and basic pH

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Abstract Poly(isobutyl cyanoacrylate) (PIBCA) monolayers, unlike those of most substances, respond to increased temperature with a decrease in area per monomer unit and a fall in the surface pressures at which surface phase transition and collapse occur. These effects are associated with an increase in entropy during isothermal compression of the film, and are attributed to the rise in temperature causing loss of solvation water, rather than to increased solubility of PIBCA.

Key words Poly (isobutyl cyanoacrylate) – monolayers – isotherms – thermodynamic parameters

Introduction

Owing to its biodegradability and biocompatibility, poly(isobutyl cyanoacrylate) (PIBCA) is being increasingly used for nanoparticle drug formulations. It is, accordingly, of interest to study its surface behavior and other physicochemical properties which are largely what govern the distribution of nanoparticles in the body [1–3].

In previous work [4], we found that the surface behavior of poly(isobutyl cyanoacrylate), like that of certain other polymers [5], certain fatty acids (including 17-methyloctadecanoic acid) [6] and tetradecanol [7], is anomalous in that, for fixed surface pressure, the area of a PIBCA monolayer decreases with increasing temperature (whereas normal behavior is for film area to increase with increasing temperature as a result of the increased flexibility of the hydrophobic chains of the molecules of the film). This kind of anomalous behavior is generally attributed to irreversible loss of molecules from the interface through evaporation or solubilization; to time-dependent relaxation processes; or to the hydration and dehydration of polar groups.

In this paper, we report a more exhaustive study of the temperature-dependence of the behavior of PIBCA monolayers spread at the air/water interface.

Experimental part

PIBCA was prepared by Couvreur et al.'s [8] emulsion polymerization method: isobutyl cyanoacrylate monomer was emulsified with water at pH 3, the hydroxyl ions of which then initiated polymerization. High-resolution gel permeation chromatography showed the mean molecular mass of the polymer so obtained to be 809 g/mol.

PIBCA dissolved in tetrahydrofuran was deposited with a Raining electronic micropipette on thermostatted Theorell–Stenhagen buffers prepared with water of resistivity 18 MΩ.cm from a Milli-RO, Milli-Q reverse osmosis system (Millipore). After deposition, films were left for 10 min before compression began.

Isothermal curves of surface pressure (π) against monomer unit are a (A) were obtained using a KSV 5000 Wilhelmy plate balance with a platinum foil plate and a Teflon trough mounted on an aluminum base with channels through which water circulates for temperature control. The curves were recorded, with a reproducibility of ± 0.5 Å^2/monomer unit, at a barrier speed of 150 mm/min (preliminary experiments showed that the curves were not affected by varying barrier speed over the range 75–150 mm/min).

Results

Effect of temperature on the π-A curves

At pH 6

The π-A curves recorded at pH 6 all exhibited three regions, reflecting an expanded state with a compressibility of the order of 10^{-2} m/mN at areas greater than 20 Å^2/monomer unit; a condensed state with a compressibility one order of magnitude lower at areas less than 10 Å^2/monomer unit; and, in between, a highly compressible transition state corresponding to a plateau of the π-A curve (Fig. 1). Raising temperature shifted the π-A curves to smaller areas, not only at high surface pressures (at which the film might be expected to lose polymer molecules into the subphase through solubilization), but also in the low surface pressure region in which the film is in its expanded state. Raising temperature also reduced the surface pressure of the transition region and increased the area range covered by the plateau; and decreased both the surface pressure and the area at which collapse began.

At pH 2 and pH 10

The effect of temperature at pH 2 and pH 10 (Figs. 2 and 3) is generally similar to that observed at pH 6. In both cases, raising the temperature reduces the film area per monomer unit. The only differences of note are that the decrease in the area of the expanded film is quite small at pH 2, but considerable at pH 10, and that the fall in the surface pressure of the plateau with rising temperature is much more pronounced at pH 2 than at pH 10. The response of the condensed film to temperature changes is practically the same at both pH values.

Joint effect of temperature and pH

The above behavior, which is the opposite of that exhibited by most substances [9–13], is also reflected in Figs.

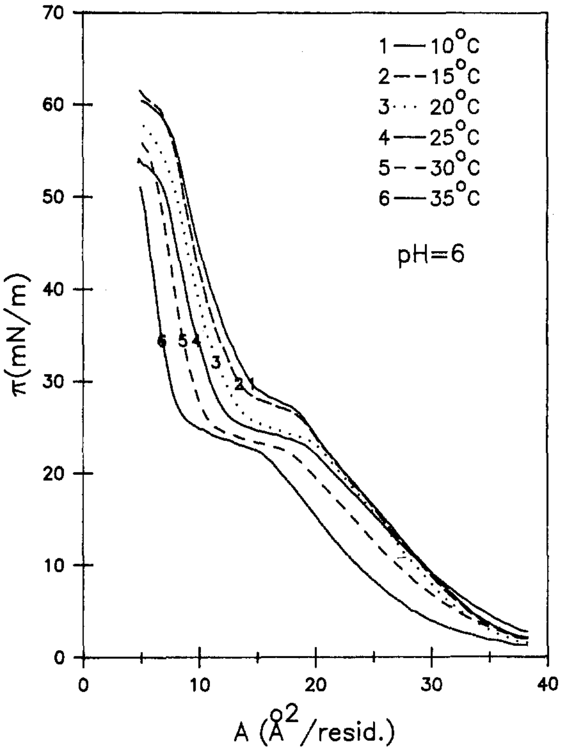
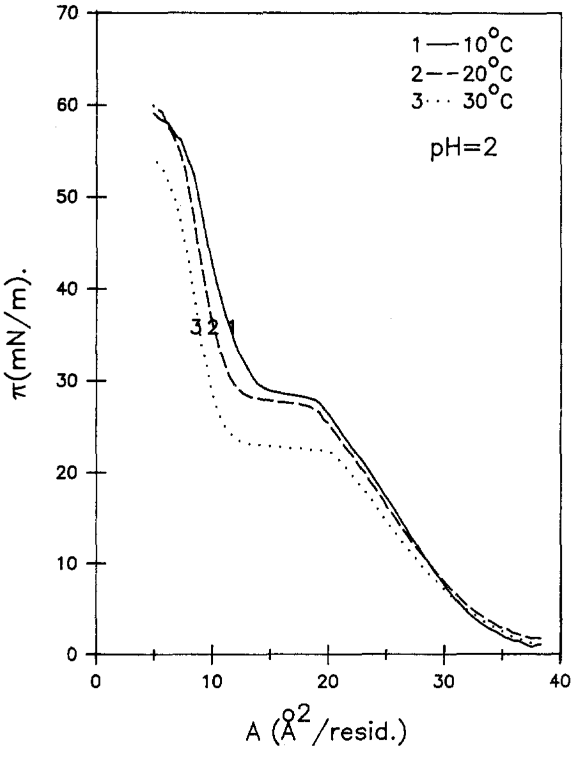


Fig. 1 Influence of temperature on the π-A isotherms of poly(isobutylcyanoacrylate) at pH 6

Fig. 2 Influence of temperature on the π-A isotherms of poly(isobutylcyanoacrylate) at pH 2



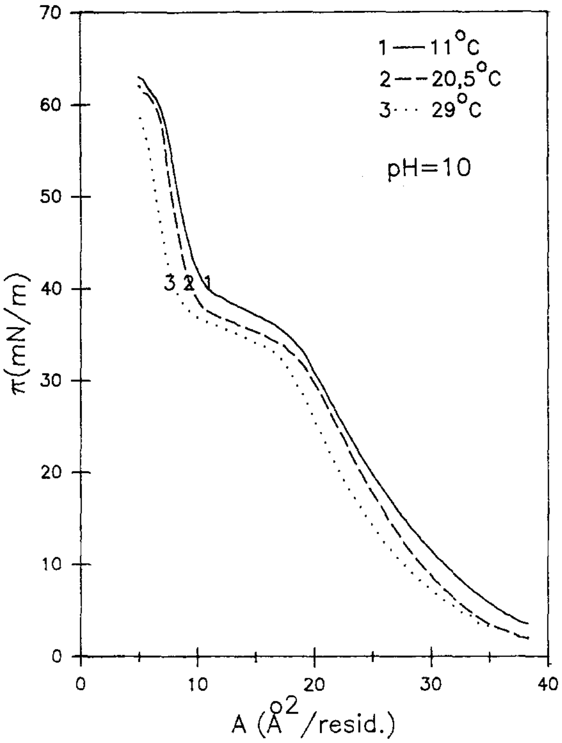


Fig. 3 Influence of temperature on the π-A isotherms of poly(isobutylcyanoacrylate) at pH 10

4A–D. In addition, Figs. 4A and B make it clear that the greatest effect of temperature on surface area occurred at pH 10 for expanded films (Fig. 4A) and at pH 6 for condensed films (Fig. 4B), though in the latter case the difference in temperature-sensitivity with respect to films of pH 2 or 10 was quite slight. Similarly, Figs. 4C and D make it evident that the plateau pressure π_t (Fig. 4C) and the collapse pressure π_c (Fig. 4D) vary less with temperature at pH 10 than at pH 2 or pH 6 (although the variation of π_c at pH 10 is appreciably greater than that of π_t at this pH).

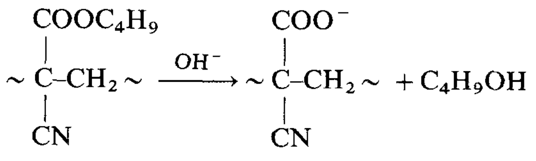
Thermodynamic parameters

To further investigate the anomalous response of PIBCA films to changes in temperature, we calculated the work done in compressing the films to collapse from a surface pressure of 2.2 mN/m (π_1) as the area under the π-A curves between the corresponding ordinates (which vary with pH and temperature). This calculated work (which included both energy of compression *sensu stricto* and the energy required for transition from the expanded to the compressed state) was identified with the Gibbs free energy of compression, ΔG_c (measurement of ΔG_c in this way would strictly require that compression had started with the film in the gaseous state of surface pressure less than 0.01 mN/m [14], but this was beyond the possibilities of our equipment). ΔG_c was always positive, increased with pH, and decreased with rising temperature (Table 1). Table 1 also shows values of the entropy of compression ΔS calculated from ΔG_c by means of the Gibbs-Helmholtz equation, and of the enthalpy of compression ΔH calculated from the equation $\Delta G_c = \Delta H - T\Delta S$; both were always positive, greatest at pH 6, and least at pH 2.

Discussion

A priori, the cause of the observed decrease in film area with increasing temperature might be thought to be an increase in the solubility of PIBCA. In that case, however, the film area ought to be considerably smaller at pH 10, at which pH PIBCA is charged as the result of the hydrolysis reaction shown in scheme I [15], than when it is uncharged (at pH 2), since ionic compounds are more soluble in water than non-ionic compounds. Although the area of the condensed film is indeed slightly less at pH 10 than at pH 2 (Fig. 4B), this is certainly not so for the expanded film (Fig. 4A); this difference in behavior between the expanded and condensed films cannot be attributed to the effect of increased solubility being outweighed at pH 10 by the effect of electrostatic repulsion between the charged carboxylate groups of the polymer, because the latter effect would be greater in the condensed film, which would therefore seem much more likely than the expanded film to have a larger area at pH 10 than at pH 2. Furthermore, any marked increase in the solubility of PIBCA with increasing temperature ought to show up in the π-A curves as an increase in film compressibility, which does not, in fact, occur (Figs. 1–3).

Rather than to the loss of PIBCA molecules due to solubilization, the anomalous temperature-dependence of the monomer area of PIBCA films seems to be more feasibly attributable to the loss of solvation water, which must also increase with temperature. Since solvation is greater at pH 10 than at pH 2, it is reasonable – and in agreement with experiment (Fig. 4A) – that the effect of temperature-induced loss of solvation water on film area be greater at the higher pH for expanded films, in which the relatively large intermolecular distances minimize the



$$\sim\underset{\displaystyle CN}{\overset{\displaystyle COOC_4H_9}{C}}\!-CH_2\sim \xrightarrow{OH^-} \sim\underset{\displaystyle CN}{\overset{\displaystyle COO^-}{C}}\!-CH_2\sim \; + C_4H_9OH$$

Scheme I. Hydrolysis of PIBCA in basic media.

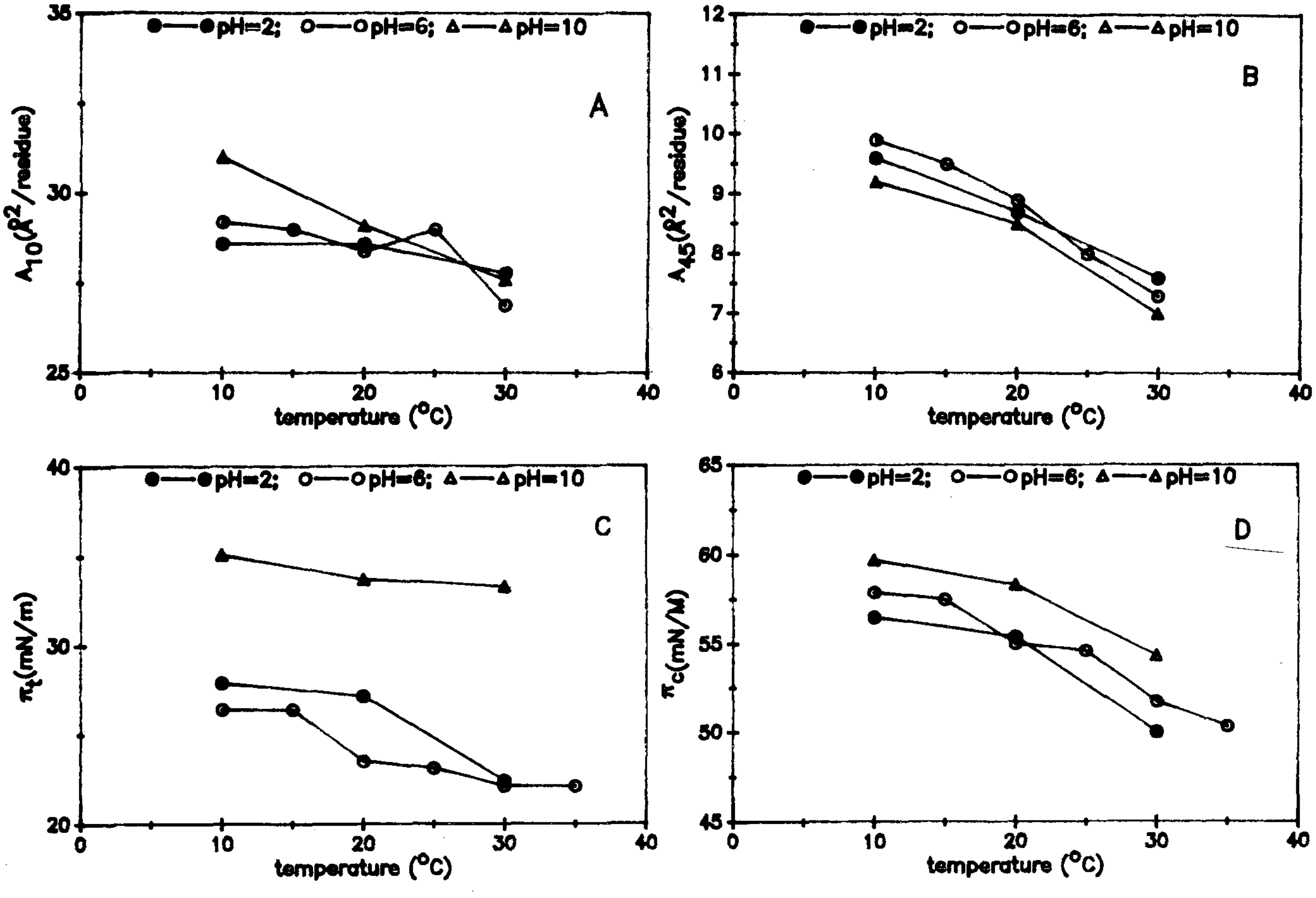


Fig. 4.A Influence of temperature on the area (per monomer unit) of poly(isobutylcyanoacrylate) films at a surface pressure of 10 mN/m. **B** Influence of temperature on the area (per monomer unit) of poly(isobutylcyanoacrylate) films at a surface pressure of 45 mN/m. **C** Influence of temperature on the surface pressure of poly(isobutylcyanoacrylate) films at the surface phase transition (the plateau in Figs. 1–3). **D** Influence of temperature on the surface pressure of poly(isobutylcyanoacrylate) films at collapse

Table 1. Thermodynamic parameters associated with the compression of poly(isobutylcyanoacrilate) films at various pH and temperatures, and data associated with their calculation

Temperature (°C)	π_1 (mN/m)	π_{colap} (mN/m)	A_1 (Å^2/res)	A_{colap} (Å^2/res)	Area under curve	ΔG_c cal/mol	ΔS cal/°K mol	ΔH cal/mol
pH = 2								
10	2.2	55.7	35.1	7.3	642.4	924.7	6.3	2707.6
20	2.2	55.4	36.9	7	631.6	909.2	6.3	2755.1
30	2.2	50.3	35.8	6.6	554.5	798.2	6.3	2707.1
pH = 6								
10	2.2	57.9	38.4	7.1	672.7	968.4	9.8	3741.8
15	2.2	57.6	38.4	7.3	645.4	929	9.8	3751.4
20	2.2	55	36.4	6.7	628.4	904.6	9.8	3776.0
25	2.2	54.7	38.4	6.6	613.4	883	9.8	3803.4
30	2.2	51.7	38.4	5.6	568.8	818.8	9.8	3788.2
35	2.2	50.3	38.4	5.1	482.6	694.7	9.8	3713.1
pH = 10								
10	2.2	60.1	38.4	6.6	803.2	1156.2	6.8	3080.0
20	2.2	59.4	38.4	6.5	756.4	1088.8	6.8	3081.0
30	2.2	57.2	38.4	5.4	708.5	1019.8	6.8	3080.2

increase in electrostatic repulsion consequent upon desolvation, while for condensed films, whose packing must be virtually independent of pH (since greater electrostatic repulsion at high pH will be offset by the greater tendency of the charged groups to become immersed in the subphase), temperature-induced loss of solvation water and the consequent reduction in film area must also be virtually independent of pH (again in agreement with experiment; Fig. 4B).

The above interpretation is supported by the results of our thermodynamic calculations, which in spite of the approximations noted in the Experimental section, would seem to be sufficiently accurate for the present discussion. ΔG_c increases with pH because the dissociation of the PIBCA means, firstly, that in compressing the film work must be done against electrostatic repulsion, and, secondly, that a greater amount of solvation water must be expelled from the film, but at constant pH this falls with increasing temperature, giving rise to positive values of ΔS and ΔH, the variations in entropy and enthalpy during film compression. The overall increase in entropy is only explicable if the increase in the collective order of the PIBCA molecules caused by film compression is offset by a decrease in the order of some other component of the system: namely, the solvation water, which loses its ordered association with the polar groups of PIBCA (it is known that solvation upon film spreading is accompanied by a decrease in entropy) [16]. The fact that ΔS is greater at pH 6 that at pH 10 may be because, although there is more solvation water at pH 10 than at pH 6, more is lost upon compression at the latter pH, at which ion-dipole attractions are not so strong as at pH 10.

Further support for the hypothesis that the anomalous response of PIBCA films to temperature changes is chiefly due to the expulsion of some of the coordinated solvation water from the vicinity of the charged regions of the polymer might be obtained by studying the behavior of the films on substrates containing substances which modify the structure of water present in the subphase. The findings of Lo Nostro and Gabrielli [17] concerning hexadecanol films on aqueous solutions of urea or saccharose are relevant in this respect.

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References

1. Douglas SJ, Illum L, Davis SS, Kreuter J (1984) J Colloid Interface Sci 101:149
2. Grislain L, Couvreur P, Roland M (1985) STP Pharm 1:1038
3. Vansnick L, Couvreur P, Christiaens-Leyh D, Roland M (1985) Pharm Res 1:36
4. Miñones J, Yebra-Pimentel E, Iribarnegaray E, Conde O, Casas Parada M (1993) Colloids and Surfaces 76:101
5. Isemura T, Hamaguchi K (1953) Bull Chem Soc Japan 26:425
6. Asgharian B, Cadenhead DA (1990) J Colloid Interface Sci 134:522
7. Caminati G, Senatra D, Gabrielli G (1991) Langmuir 7:604
8. Couvreur P, Kante B, Roland M, Guiot P, Baudin P, Speiser P (1979) J Pharm Pharmacol 31:331
9. Phillips MC, Chapman D (1968) Biochim Biophys Acta 163:301
10. Cadenhead DA, Demchak RJ, Phillips MC (1967) Kolloiz Z. Polymere 220:59
11. Dörfler HD, Rettig W (1980) Colloid Polym Sci 258:839
12. Asgharian B, Rice DK, Cadenhead DA (1989) Langmuir 5:30
13. Fidelio GD, Maggio B, Cumar FA (1986) Biochim Biophys Acta 854:231
14. Gershfeld NL (1976) Annu Rev Phys Chem 27:349
15. Lenaerts V, Couvreur P, Christiaens-Leyh D, Joiris E, Roland M, Rollman B, Speiser P (1984) Biomaterials 5:65
16. Hührenfuss H, Alpers W (1983) J Phys Chem 87:5251
17. Lo Nostrono P, Gabrielli G (1993) Langmuir 9:3132