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An Investigation of Dilute Aqueous Solution Behavior of Poly(oxyethylene) + Poly(oxypropylene) + Poly(oxyethylene) Block Copolymers

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Dilute solution phase scanning microcalorimetric transition data for 27 members of the pluronic ABA block copolymer family are presented. Analysis of these data suggest a correlation between thermodynamic parameters for the observed transitions and poly(propylene oxide) content.

Introduction

In recent communications we have reported studies of conformational transitions in dilute aqueous solutions of a number of ABA block copolymers.¹⁻⁵ These investigations have presented high sensitivity differential scanning calorimetry (HSDSC), variable temperature nuclear magnetic resonance spectroscopy (NMR), isothermal calorimetric, densimetric, and X-ray data obtained for members of the pluronic group of surfactants of the general formula shown:



The physical properties of these polymers as solids or in relatively concentrated solutions have been exploited in the formulation of aqueous preparations of emulsions and creams and the preparation of nonwater-soluble cosmetics and drugs and have been reviewed extensively.⁶⁻⁹ These block copolymers are of interest both due to their practical applications, and from a fundamental perspective addressing hydrophobic-hydrophilic interactions, cloud points, gelation phenomena, and critical micelle concentrations.

While micellar solutions of block copolymers have been investigated by the techniques of NMR,¹⁰⁻¹² light scat-

tering,¹³⁻¹⁹ fluorescence,^{20,21} SANS,^{15,22-23} and DSC,^{15,24} these reports are usually of analyses carried out on solutions of >1% w/v polymer concentration. At these concentrations, reported DSC analyses show broad transition ranges and large endothermic heats of micellization.

More recent reports of the aggregation behavior of these block copolymers, although usually related to the micellization of these systems at concentrations in excess of 1% w/v, suggest the formation of an aggregate with a POP core and a POE "palisade" layer.²⁴

Although these aggregates are usually called micelles, at low solution concentration (0.1-1% w/v) the polymer is believed to exist as a monomer, whereupon heating the block copolymer is believed to associate to form poorly defined systems where aggregation numbers are reported to be uncertain or small.²⁵⁻²⁸

We have now extended our study of the pluronics to include 27 examples and have used the techniques of HSDSC, temperature-controlled NMR, and light scattering and vapor phase osmometry to investigate the dilute aqueous solution behavior (<1% w/v) of these polymers.

Materials and Methods

Samples of the pluronics studied were donated by ICI (Cleveland, U.K.). Their purity was established by the presence of a single elution peak by GPC (refractive index detection). Solutions were prepared by dissolution of the pluronic in doubly distilled water at a mass concentration of 5 mg cm⁻³. Solution phase HSDSC measurements were conducted in a Microcal MC2 microcalorimeter (Microcal, Amhurst, MA). The temperature

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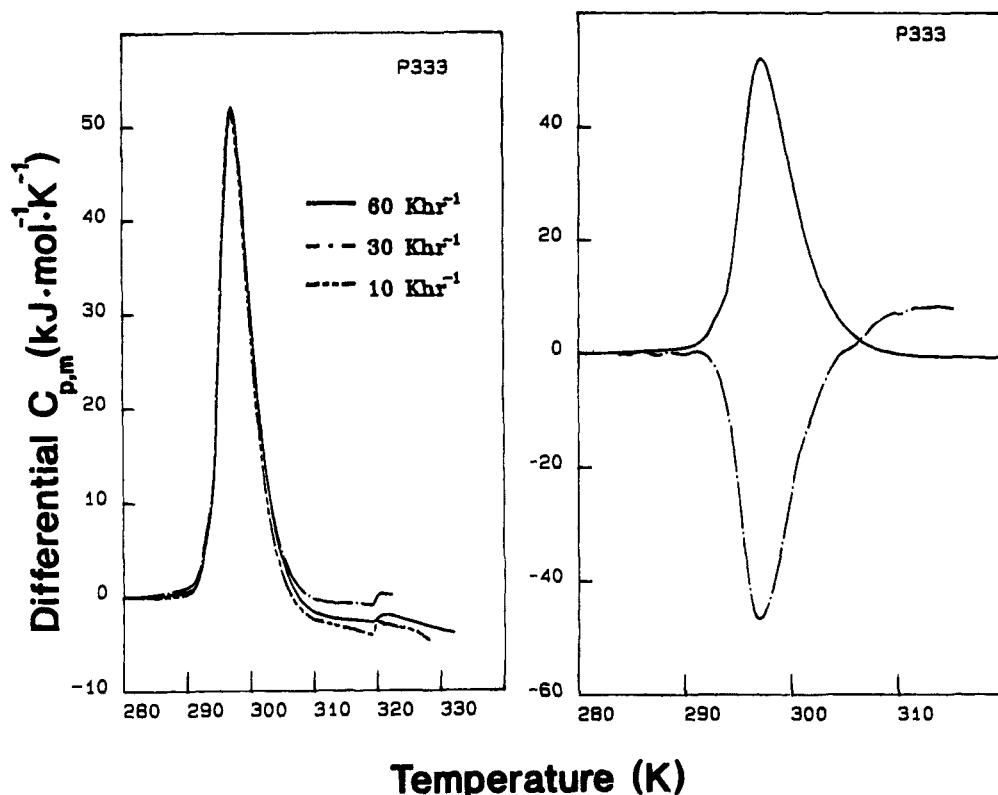


Figure 1. Temperature dependence of the partial specific heat capacity, C_p , for the pluronic P333 at HSDSC scan rates of 10, 30, and 60 Khr^{-1} and heating and cooling scans for P333 at 30 Khr^{-1} .

dependence of the differential specific heat capacity as a function of temperature was determined at a scan rate of 0.017 K s^{-1} . Instrumental control and data acquisition were controlled by dedicated software (DA2, Microcal). Calibration was by the electrical substitution method.

^{13}C and ^1H chemical shift NMR measurements were carried out on a 270 MHz JEOL GX spectrometer using samples identical to those analyzed by HSDSC. Temperature measurements are accurate to $\pm 0.3^\circ\text{C}$. All shifts were calibrated against an aqueous solution of sodium 2,2-dimethyl-2-silapentane-5-sulfonate held in the inner capillary of a 5 mm coaxial tube.

Vapor phase osmometry was performed on samples of concentrations identical to those used in NMR and calorimetric studies. Temperature-controlled light scattering measurements were performed on a Sofica 4200. Diode Array UV spectrometry was performed on a Hewlett-Packard 8452A.

Results and Discussion

Previous reports^{1,2} from our laboratory give details of the observation of phase transitions in dilute aqueous solutions of poly(oxyethylene)–poly(oxypropylene)–poly(oxyethylene) block copolymers which were occasioned by an increase in temperature. The techniques adopted for these studies were high sensitivity scanning calorimetry (HSDSC) and temperature controlled solution phase ^{13}C NMR. For the study polymer, pluronic P237, both techniques indicated a phase transition temperature in D_2O of 308 K. The interpretation of these data was based upon the assumption of dehydration of the poly(oxypropylene) moiety of the polymer as temperature increased. Indeed, the NMR evidence we presented indicates that it is a change in the relaxation time (T_1) of the methyl group in the poly(oxypropylene) moiety which reflects these changes in overall conformation. Subsequent studies by this group on the properties of this and related polymers have shown³ that the thermal behavior of the dilute polymer solutions, when subject to HSDSC investigation, relates *only* to the poly(oxypropylene) content of the polymers. There is no relationship that can be discovered

between any of the thermodynamic parameters and total molar mass nor with polyoxyethylene content.

Figure 1 shows a typical HSDSC thermogram for the block copolymer P333. It is important to note that the observed transition appears to be reversible and is not kinetically limited at scan rates from 10 to 60 K/h . The thermograms suggest hydrophobe desolvation that might be expected upon either intra- or intermolecular hydrophobic association following conformational change.^{29,30} Structures which result from this temperature-driven dehydration are as yet undefined.

For Figure 1, the T_m or transition temperature for the process can be determined as the maximum value of the excess specific heat capacity; the ΔH_{vH} or van't Hoff enthalpy (related to the transition width) and the ΔH_{cal} or calorimetric enthalpy (related to the integrated area under the C_p curve) can both be determined in units of $\text{kJ}\cdot\text{mol}^{-1}$. The cooperativity (n) can be easily derived as $n = \Delta H_{\text{vH}}/\Delta H_{\text{cal}}$. C_p is the maximum molar heat capacity in units of $\text{kJ}\cdot\text{mol}^{-1}\cdot\text{K}^{-1}$.

Dilute solution phase thermodynamic characteristics for the pluronics investigated in this study derived from HSDSC experiments are shown in Table 1. The table contains information on the eight pluronics previously reported as well as for an additional 19 pluronics.

Included in the table is a descriptive code to identify each polymer, the molar mass, the contribution of the poly(oxyethylene) groups to the molar mass, the contribution of the poly(oxypropylene) group to the molar mass, the transition temperature of the polymer (T_m), the molar heat capacity (C_p), the van't Hoff (ΔH_{vH}) and calorimetric (ΔH_{cal}) enthalpies, and the cooperativity for the transition.

It is important to note that the observed HSDSC transitions are at lower temperature than the macroscopic phase separation temperature or cloud point (CP) for these

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Table 1. Physical Characteristics for the Studied Pluronics (at 5 mg cm⁻³)^a

pluronic	<i>M</i>	<i>M</i> (PO)	<i>M</i> (EO)	<i>T</i> _m	<i>C</i> _p	ΔH_{vH}	ΔH_{cal}	<i>n</i>
P101	1100	950	150	51.03	3.3	191.2	60.6	3.2
P105	1900	950	950	73.01	1.6	196.8	32.4	6.1
P108	4800	950	3850	81.65	1.2	253.2	20.6	12.3
P122	1650	1200	450	53.49	3.9	157.1	87.2	1.8
P123	1925	1200	725	52.11	4.6	212.2	75.8	2.8
P124	2200	1200	1000	40.57	8.3	253.7	107.3	2.4
P181	2090	1750	340	30.35	13.6	227.0	183.1	1.2
P182	2400	1750	650	38.91	11.4	265.8	138.4	1.9
P184	2900	1750	1150	40.85	12.3	218.4	184.9	1.2
P188	8350	1750	6600	57.33	5.5	224.2	91.6	2.5
P207	6600	1980	4620	50.90	7.6	243.0	108.3	2.2
P215	4150	2050	2100	41.85	11.9	274.2	143.4	1.9
P217	6600	2150	4450	50.08	7.1	217.1	113.0	1.9
P231 ^b	2750	2250	500	28.35	21.8	290.3	226.7	1.3
P234	3750	2250	1500	33.43	22.5	393.8	178.7	2.2
P235	4650	2250	2400	36.21	18.7	307.7	193.5	1.6
P237	7700	2250	5450	41.65	18.2	310.3	194.3	1.5
P238	11800	2250	9550	36.95	14.8	286.4	166.1	1.7
P282	3450	2750	700	27.13	31.1	335.0	278.1	1.2
P284	4600	2750	1850	35.67	19.1	288.3	210.0	1.4
P308	13500	2700	10800	43.80	12.0	309.8	129.5	2.4
P331	3800	3250	450	19.97	59.4	446.7	379.6	1.2
P333	4950	3250	1700	25.29	52.2	462.0	334.6	1.4
P335	6500	3250	3250	27.55	45.8	439.8	313.1	1.4
P338	14000	3250	10750	31.75	22.6	309.7	226.3	1.4
P401	4400	4000	400	18.37	74.9	528.0	400.8	1.3
P407	12000	4000	8000	27.40	26.4	494.0	160.8	3.1

^a *M* = total molar mass; *M*(PO) = contribution of poly(oxypropylene) to *M*; *M*(EO) = contribution of poly(oxyethylene) to *M*; *T*_m = transition temperature (°C). ΔH_{vH} and ΔH_{cal} are, respectively, the van't Hoff enthalpy (related to the transition width) and the calorimetric enthalpy (related to the integrated area under the *C*_p curve); both are in units of kJ·mol⁻¹. The cooperativity (*n*) = $\Delta H_{vH}/\Delta H_{cal}$. *C*_p is the maximum molar heat capacity in units of kJ·mol⁻¹·K⁻¹. ^b Solution concentration of 5.6 mg cm⁻³.

polymers. We did not observe any phase separation at the study temperature range and polymer concentration used. We have, however, presented elsewhere a theoretical approach to the determination of both the low temperature phase transitions reported in Table 1 and the higher temperature transitions related to the cloud point, which were not determined experimentally in this study.⁴

In all cases the phase transitions observed for these pluronics are best related to the poly(oxypropylene) portion of the ABA triblock polymer. Correlations between mass of the poly(oxypropylene) portion of the polymer and calorimetrically measured enthalpy for the dilute solution phase transitions are presented in Figure 2.

The data displayed in Table 1 represent the most comprehensive set of data available for these ABA block copolymers. These data reveal the general trends as noted previously—and as described in correlation equations more recently.³¹

However, as with all correlations, it is more satisfying to analyze the data in a way that invests the conclusions with some physical significance. We therefore have analyzed this more substantial data set to explore the possibility that there is an underlying uniformity in the behavior of these polymers or that the existence of specific polymer types, i.e. those polymers which contain the same fraction of ethylene oxide but have varying total molar masses, is differentiable from polymers having a different fraction of ethylene oxide content. The data in Figure 3 have been produced by calculating the average calorimetric enthalpy associated with a propylene oxide unit for each

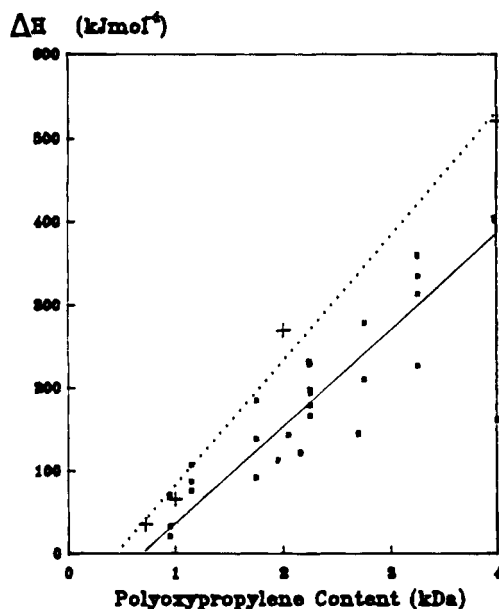


Figure 2. Calorimetric enthalpy (ΔH_{cal}) versus poly(oxypropylene) content (mass in kDa) of pluronics. (■ = pluronics, + = poly(oxypropylene)).

of the differing series of polymers. The series members are identified as those polymers containing the same fraction of ethylene oxide but which have varying total molar masses. This calculation effectively assigns the total calorimetric enthalpy to the propylene oxide portion of the polymers, and this is in line with all previous reports of our experimental observations derived from both HSDSC data and from other experimental techniques (e.g. scanning densimetry, NMR). The excellent linearity (regression coefficient -0.992) suggests that indeed there is a unifying behavior which aligns the HSDSC data for these 27 polymers in a systematic fashion. Of course the slope of this plot is, then, the average enthalpy per propylene oxide unit per fraction of ethylene oxide content—and this shows how the **magnitude** of this enthalpy depends upon the ethylene oxide fraction but how the **change** in enthalpy is dependent upon the propylene oxide content. The intercept value of approximately 5 kJ (unit of propylene oxide)⁻¹ may, therefore, be regarded as the calorimetric enthalpy per propylene oxide in the absence of **any** ethylene oxide. It appears, therefore, that the relationship displayed in Figure 3 does indeed provide a means of systematizing the behavior of all the pluronics and that it offers some means of predicting properties of poly(oxypropylene)-based polymers.

Likewise, investigation of the HSDSC observed phase transitions for dilute solutions of poly(oxypropylene)-only polymers allows correlation³¹ of the calorimetric enthalpy associated with phase transition per unit of propylene oxide against polymer molar mass (Figure 2).

Values in this paper are reported for solutions of 5 mg cm⁻³ of polymer in pure water. Phase transition temperatures for P237 (41.6 °C at 5 mg cm⁻³ in H₂O) can be influenced by solvent (35.2 °C at 5 mg cm⁻³ in D₂O) and by the presence of other dissolved species (33.9 °C at 5 mg cm⁻³ in 0.03 M phosphate buffer). Concentration also influences the observed dilute solution transition temperature for these polymers (39.7 °C at 10 mg cm⁻³ in H₂O).

To test whether the relationship of transition temperature to poly(oxypropylene) content for the series would be substantially affected by a change in solution concentration, scanning calorimetric data were obtained at a standard polymer concentration of 5 mg cm⁻³ and com-

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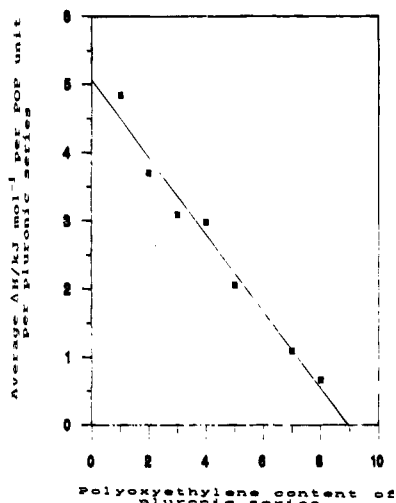


Figure 3. Average calorimetric enthalpy (ΔH_{cal}) per poly(oxypropylene) (POP) monomer unit for each series (series members having the same poly(oxyethylene) content) versus poly(oxyethylene) (POE) content as indicated in the last digit of the pluronic code (Table 1).

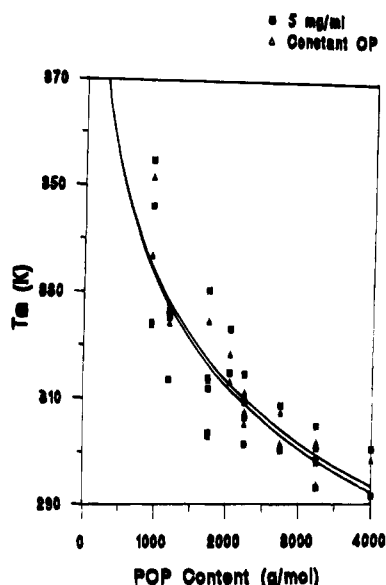


Figure 4. Phase transition temperature (K) versus poly(oxypropylene) (g/mol) content at a concentration of 5 mg cm⁻³ (■) and at constant poly(oxypropylene) (POP) concentration (▲).

pared with data obtained at constant poly(oxypropylene) concentration (overall concentration range of 5–26 mg cm⁻³). These data are presented in Figure 4 and suggest that, across the series, the correlation between poly(oxypropylene) content and thermodynamic parameters is maintained, in spite of varied overall solution concentration.

As noted above, the earlier publications on the temperature controlled conformations of these block copolymers described the observed transitions in dilute (0.1–1%, w/w) aqueous solution in terms of the dehydration of the polymer that occurred as a result of the increase in temperature and the consequent rearrangement of solvation water resulting from changes in polymer–water interactions. We have also recently reported the observation of changes in polymer solution structure as a result of time-driven phenomena. Output from an isothermal microcalorimeter upon study of a 0.5% w/w aqueous solution of pluronic P237 and of P238 shows, superficially, the appearance of p - t curves that resemble the profile

anticipated for an autocatalytic reaction.³² These calorimetric results for the enthalpies (approximately -9 kJ mol⁻¹) are associated with a relaxation process related to conformational changes upon slow hydration of the polymer following the departure of a molecule from the solid phase into solution. The conformation of the polymer molecule entering solution is not the equilibrium structure and hence relaxes to its preferred orientation upon interaction with water. The results reported in this study were conducted at the low concentration and at the low-temperature side of the corresponding scanning calorimetric transition for the studied polymers. Thus we presume they reflect unimolecular processes. As such, NMR analysis was attempted to try to correlate the isothermal calorimetric results with a specific molecular region of the linear polymer. Observation of carbon nuclei performed on both 270 and 400 MHz instruments failed to show any significant differences over time for dilute solutions of P237 in D₂O.

Light scattering measurements of particle mass and high precision density measurements of partial molar volumes reveal that a temperature driven aggregation process does occur for pluronic P237. At the study temperature of 25 °C, the system is largely monomeric ($M_w = 2430$, corresponding most closely with the poly(oxypropylene) content) with a very small proportion of aggregate present. Upon heating of the sample to 37 °C, particle mass dramatically increases but this increase in size does not result in the cloud point phenomenon that occurs at higher temperature.

The monomolecular nature of these polymers in dilute solution below the phase transition temperature is further supported by vapor phase osmometry measurements. These measurements, on solutions identical to those used in the microcalorimetric experiments, suggest, for example, that the apparent dilute solution molar mass of P407 at 35 °C is 4829 (see Table 1 for actual values) and the apparent molar mass of P237 under the same conditions is 3841.

These values are smaller than the total molar mass of these polymers. Thus, we assume they reflect the monomeric nature of these polymers in dilute solution and perhaps indicate a colloidal poly(oxypropylene) core (observable by light scattering measurements) surrounded by solution phase poly(oxyethylene).

Discrimination between these two domains within the linear polymer is reinforced by analysis of the differences between the van't Hoff enthalpy, which is related to the scanning calorimetric transition width, and the calorimetric enthalpy, which is related to the integrated area under the heat capacity curve. Comparison of these enthalpic terms has led to the identification of independent melting domains within molecules under calorimetric scrutiny.³³ In this case, a value close to 2 occurs, over the whole series of pluronics, for the ratio of van't Hoff to calorimetric enthalpies. This may imply that the center of the melting colloidal poly(oxypropylene) core may behave differently from the poly(oxypropylene) associated with the external poly(oxyethylene) polymer chain (and hence "in solution") at the phase transition temperature.

Finally, principal component and cluster analyses were performed on the data shown in Table 1 by using the program TSAR (Oxford Molecular) run on a Silicon Graphics Indigo system. Although the dendrogram shows no remarkable features, it is possible to represent 93% of the total variance of these data using the first two principal

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components. This two-dimensional plot showed no major groupings of the copolymers but a gradual arrangement of the data according to a decrease in the value of the second-component score with increase in the EO content. Such behavior supports the relationship illustrated in Figure 3 that there is no major distinction among the different polymers but a gradual change in their solution properties as a function of their composition.

Summary

The description of the two-domain polymeric structure described above, taken together with the relationship of poly(oxypropylene) content of these polymers to phase transition temperature, and the monomeric nature of these ABA block copolymers in dilute solution below their phase transition temperature, suggests that the observed phase transition is an event related to hydrophobic aggregation, but independent of the polymer cloud point. A hypothesis in broad agreement with other workers is that of a coiled colloidal poly(oxypropylene) core surrounded by the solvated poly(oxyethylene) portion of the molecule, sectioning the polymer into a hydrophobic central domain and a hydrophilic outer region. Upon temperature-induced phase transition at these concentrations, the central poly(oxypropylene) core must associate to produce larger aggregates.

It is important to note that we have observed the phase transitions of P237 and P407 in a temperature scanning diode array ultraviolet/visible spectrometer. Plots of the observation wavelengths (220 and 250 nm, respectively) against temperature are shown in Figure 5 with the first derivatives of the spectra shown as insets. Transition temperatures taken from these first-derivative spectra are 41.6 for P237 and 27.8 °C for P407 (within 0.4 °C of the value in Table 1 in the worst case). This technique may represent an alternative to DSC analysis for the determination of thermal characteristics of these pluronics.

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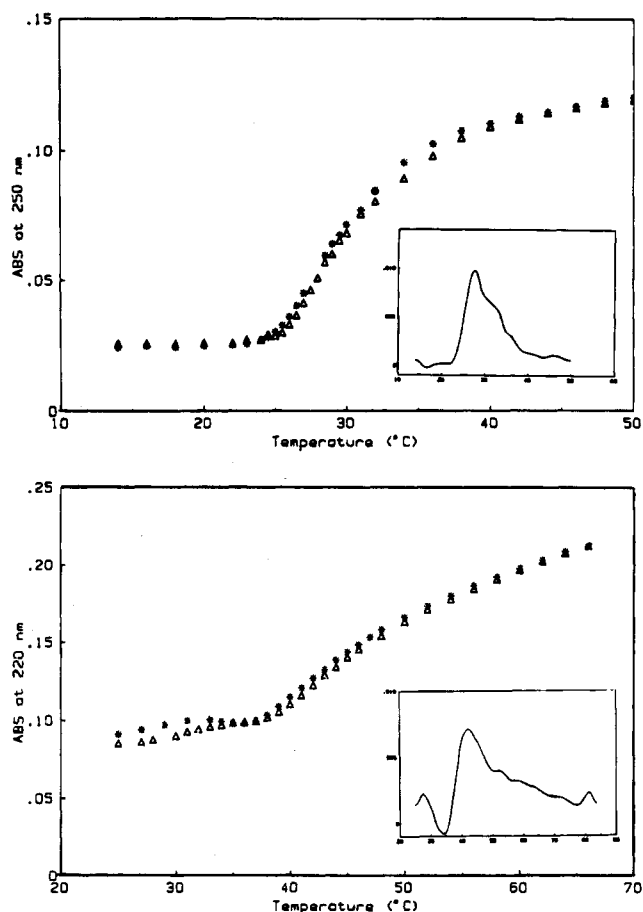


Figure 5. (a, Top) Diode array UV analysis of P407 from 10 to 50 °C at 250 nm (Δ = heating; * = cooling). (b, Bottom) Diode array UV analysis of P237 from 20 to 70 °C at 220 nm (Δ = heating; * = cooling).

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