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Thermodynamics of the partitioning of poly(propylene oxide) between aqueous and chlorinated organic phases compared to poly(ethylene oxide) and other hydrophilic polymers†

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ABSTRACT: Thermodynamic functions associated with the partitioning of poly(propylene oxide), PPO, between aqueous and organic (chloroform, dichloromethane, and chlorobenzene) phases were determined and analyzed in comparison with those for the partitioning of poly(ethylene oxide), PEO, and poly(vinyl pyrrolidone), PVP. Amounts of water accompanying the partitioning of PPO to the organic phases were also measured. These results reveal that PPO partitioning is controlled by hydrophobic effects (entropic contribution), which was confirmed by the release of a significant amount of water molecules following the partitioning. Hydrophilic polymers like PVP and polyacrylamide, on the other hand, remain almost quantitatively in the aqueous phase. PEO remains a unique example of a polymer displaying high affinity for water, but that can be extracted to certain organic solvents (which should display hydrogen bond donating capacity). Copyright © 2006 John Wiley & Sons, Ltd.
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KEYWORDS: polymer partitioning; calorimetry; hydrophilic polymers; poly(propylene oxide)

INTRODUCTION

Poly(ethylene oxide), PEO, is a widely studied polymer due to its varied applications in industrial, cosmetic, and biomedical products.[1] Moreover, its solution properties have been the focus of many investigations producing some results which point to an elusive character that led Israelachvili to refer to ''the different faces of poly(ethylene glycol).''[2] These different faces account both for its surprisingly high solubility in water, especially if compared to the other homologs, poly(methylene oxide) and poly(propylene oxide), which display quite reduced water solubility. On the other hand, PEO is also soluble in polar organic solvents, displays some surface activity in polar solvents and can be attracted to hydrophobic surfaces.[2] These features are of relevance for a variety of potential applications of PEO, especially for biomedical purposes.[1,3]

This behavior is also reflected in a statement by Bailey and Koleske,[4] that ''. . .PEO. . . is totally extractable from water solution to chloroform. The extraction by chloroform must be due in part to a high entropic contribution since the extraction involves disordering of local helical conformations of PEO chains and a gain in entropy with respect to water as a solvent.''

This statement prompted a series of investigations by our group, whose main results may be summarized as follows:

- partitioning of PEO between aqueous and organic ($CHCl_3$ and CH_2Cl_2) phases depends on its molar mass, being it almost quantitatively transferred to the organic phases at higher molar masses, resulting from the decrease in end group contributions;[5,6]
- PEO is not extracted to chlorobenzene phases, which has been ascribed to the lack of hydrogen bond donating capacity of this organic solvent;[6]
- PEO partitioning is endothermic and, hence, must be entropically driven;[6]
- a significant amount of water molecules are released from their role of solvating PEO as it is transferred to the organic phases, and this release is ascribed as being the origin of the entropy increase.[6]

Some of these findings were more recently confirmed by the report of an investigation on the partitioning of PEO between aqueous and fluorinated organic phases.[7]

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The study reported here presents new data on the partitioning of PEO, but also extends the same systematic investigation to the partitioning of poly(propylene oxide), PPO, producing thermodynamic data which are discussed in comparison to those for PEO. Partitioning of other hydrophilic polymers, poly(vinyl pyrrolidone), PVP, and poly(acrylamide), PAM, is also investigated.

EXPERIMENTAL

Materials

The polymers used in this study were: PEO 300, 400, 1500, and 4600 (from Aldrich), PEO 6000 (from Riedel), PEO 600, PEO 1000, PEO 3350, and 10 000 (from Sigma), PEO 35 000 (from Fluka), PPO 425, 725, 1000, 2000, 2700, and 4000 (from Aldrich), PVP 10 000 and 55 000 (from Aldrich) and poly(acrylamide), PAM, 1500 g mol^{-1} (from Aldrich). All polymers were used without further treatment.

Water used throughout was deionized and of Milli-Q grade. Dichloromethane and chloroform (from Merck) were refluxed over $CaCl_2$ (previously activated at 170 °C, for 24 h), distilled under N_2 and kept over molecular sieves. Chlorobenzene, from Merck, was used without treatment.

Determination of partition coefficients

Biphasic systems were prepared by dissolving the polymers in organic solvent (PPO), or in water (PVP and PAM), then adding the second phase. The amount of polymer was kept as 0.5 wt% (global composition), except for PAM, whose concentration was 56 wt%. These systems were shaken and left in a water bath at 25 °C (±0.01) for at least 15 days. A previous kinetic investigation confirmed that this time was enough to ensure equilibrium. Aliquots of both phases were withdrawn and dried at 60 °C until constant weight, which also allowed derivation of their partition coefficients. For systems with more extreme K values, care was taken in adjusting the volume of phases and aliquots so that final polymer masses were always greater than 1 mg. With PVP, after drying, the polymer content was assayed using the colorimetric method proposed by Levy and Fergus[8] and a Beckman DU 640 B spectrophotometer, at 500 nm.

All partition coefficients are expressed as the ratio of mole fractions in the organic over the aqueous phase, calculated on a monomer basis.

Calorimetric measurements

Transfer enthalpies were determined directly using a titration calorimeter VP-ITC (MicroCal, Inc, USA). Systems were prepared as described for the determination of partition coefficients. After equilibrium, the phases were separated and one of them added to the calorimeter cell (volume of 1.436 mL), operating at 25 °C. During these experiments, aliquots of 3–15 μL of the other phase (to which an excess of polymer was added) were injected consecutively and the heat exchanged recorded. Enthalpy values were calculated using the actual number of moles transferred during each injection, calculated with the aid of the previously determined partition coefficients. Phases were selected so that the phase where most of the polymer was found was placed in the cell, and the other in the syringe, maximizing the energy exchanged per injection.

Typically 15 injections were made for each experiment. Averages were determined using at least two independent titrations and deviations of the derived enthalpy values were smaller than 7%.

This procedure was tested against that used previously[6] for the partitioning of PEO 3350, producing similar precision and values that were in agreement within their uncertainties. The titration method, however, was advantageous since it was faster and required smaller samples.

Determination of water content in the organic phases

Biphasic systems were prepared as for the determinations of the partition coefficient. The amount of water in the organic phases in the presence and absence of polymer was directly determined by Karl Fischer titration using Orion AF 8 equipment, as previously described.[6]

RESULTS AND DISCUSSION

Determination of transfer enthalpies for PEO

Previous investigation[6] produced calorimetric data for the partitioning between aqueous and organic phases for PEO of three molar masses. The present investigation reports data for other PEO, and they are all shown in Fig. 1. As in the previous investigations, the data refer to the polymer transfer from the aqueous to the organic phase. These new data were determined by an alternative procedure involving direct titration of one of the phases, containing a greater amount of PEO, into the other phase. The close agreement between data from the two techniques validates this new procedure. With respect to the transfer enthalpies shown in Fig. 1, a trend similar to that displayed by the Gibbs transfer function is observed as a function of PEO molar mass (Fig. 2). An increase in PEO molar mass leads to more positive transfer enthalpies, indicating that the contribution of the EO units to the transfer is more positive than that of the hydroxyl end groups. The transfer enthalpy for one ethylene oxide unit can be estimated by the plateau values

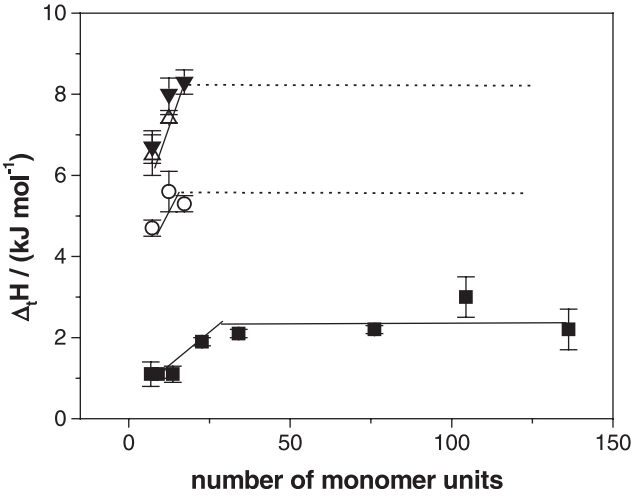

Figure 1. Transfer enthalpies for PEO and PPO between aqueous and organic phases, at 25 °C (values calculated on a monomer basis). Symbols: (■) PEO between water/chloroform; all others refer to PPO between water and (○) chloroform, (△) dichloromethane, and (▼) chlorobenzene

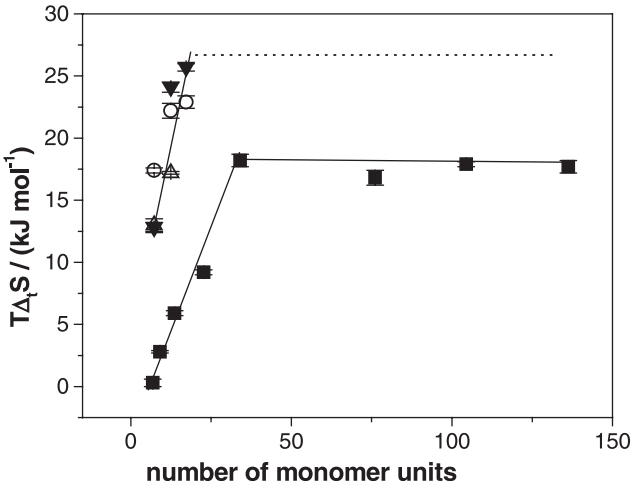

Figure 3. Entropic contributions to the transfer of PEO and PPO between aqueous and organic phases, at 25 °C (values calculated on a monomer basis). Symbols: (■) PEO between water/chloroform; all others refer to PPO between water and (○) chloroform, (△) dichloromethane, and (▼) chlorobenzene

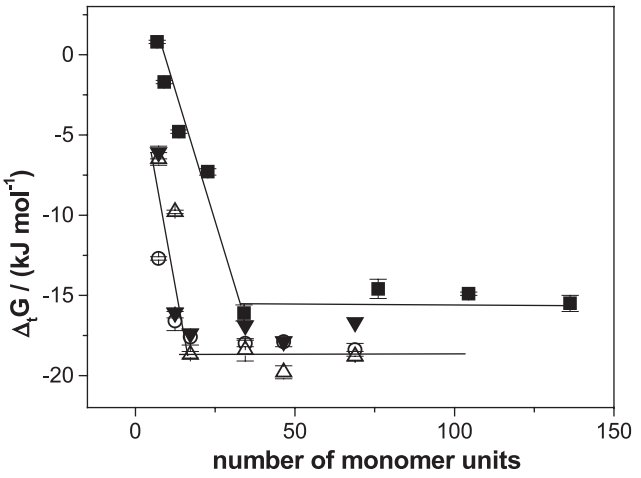

Figure 2. Gibbs transfer energies for PEO and PPO between aqueous and organic phases, at 25 °C (values calculated on a monomer basis). Symbols: (■) PEO between water/chloroform; all others refer to PPO between water and (○) chloroform, (△) dichloromethane, and (▼) chlorobenzene

in Fig. 1 as being *ca*. 2.5 and 3 kJ mol^{-1}, from aqueous to, respectively, chloroform and dichloromethane phases. Both EO and —OH groups should be less energetically solvated by the organic solvents than in water, hence the positive values, but these results also indicate that the difference between solvation energies is more pronounced for ethylene oxide units than for the hydroxyl groups. Only two PEOs were studied with chlorobenzene phases,[6] but all values are significantly more positive than those determined with the other chlorinated solvents, which has been ascribed to the lack of hydrogen bond donating capacity of this solvent.

The values for the transfer entropies, derived from the enthalpy and Gibbs function values, are shown in Fig. 3. Again, the same trend of variation with PEO molar mass is observed, indicating a more positive entropic contribution for the transfer of the EO units than of the hydroxyl groups. This finding may be rationalized taking into account that this entropy increase is ascribed to the release of the water solvation molecules that were restrained in the aqueous phase and are displaced when the polymer moves to the organic phase. According to this hypothesis the present observation indicates that the organic solvent displaces more water molecules from the EO units than from the hydroxyl end groups.

Partitioning of poly(propylene oxide)

Partition coefficients determined for the partitioning of PPO of different molar masses between water and chlorinated organic phases showed the same behavior found for the partitioning of PEO: partitioning towards the organic phases becomes more favorable as the molar mass increases, until a plateau value is reached. Figure 2 compares these data in the form of Gibbs transfer energies, along with those for the partitioning of PEO, for comparison. Analysis of this figure reveals that partitioning of PPO is more favorable than that of the similar PEO. This confirms what may be expected from the assumption that PPO is more hydrophobic than PEO, since it has an extra methylene group in the repeating unit. Additionally, only a small difference is observed among the partition

coefficients for PPO in the three organic solvents, values for systems with chlorobenzene being slightly smaller, but still all are capable of efficiently extracting PPO. This is in contrast to what was observed with PEO, which only displayed favorable partitioning towards phases containing dichloromethane and chloroform. This finding may suggest that the contribution from hydrogen bonding between the organic solvent and PPO, present in phases containing chloroform and dichloromethane, but not with chlorobenzene, is not so relevant for this partitioning, which should therefore be controlled by hydrophobic contributions.

The difference between the Gibbs transfer energies for EO and PO units can be estimated at the plateaus of the two curves of Fig. 2 as *ca.* $-3\,\mathrm{kJ\,mol^{-1}}$, reflecting the contribution to the Gibbs transfer energy from a (CH_2) unit. In the related literature, this contribution has been referred to as the hydrophobic contribution, and is usually derived from studies on the partitioning of homologous series of solutes between aqueous and organic phases.[9] Typical reported values lie at around $-3\,\mathrm{kJ\,mol^{-1}}$,[9,10] in good agreement with the value determined in this study.

Partitioning data for PPO, shown in Fig. 2, also display a break in the trend of increasing partitioning coefficients with molar mass, which occurs at a lower molar mass for PPO (*ca.* $1000\,\mathrm{g\,mol^{-1}}$, equivalent to *ca.* 17 PO units) than for PEO (*ca.* $2000\,\mathrm{g\,mol^{-1}}$, or 45 EO units). Using the same interpretation proposed for the partitioning of PEO,[5,6] this break would correspond to the disappearance of contributions from the hydroxyl end groups to partitioning and defines the molar mass at which PPO loses its polyglycol character to behave like a polyether. Since this position reflects the balance between the opposing contributions of —OH groups *versus* EO or PO units, if we assume that the —OH contributions are similar for the two polymers, the different positions of this break lead to the conclusion that the PO contribution to partitioning is more important than that of EO units, consistent with the more negative value for its Gibbs transfer energy reported above.

The transfer enthalpies for some PPO were determined calorimetrically and these values are shown in Fig. 1. These values are more positive than those determined for PEO (also shown in Fig. 1, for comparison), indicating a greater difference in solvation enthalpies for PPO between aqueous and organic phases. Assuming that hydration of PEO should be more energetic than that of PPO, such a difference in transfer enthalpies could be ascribed to a less energetic solvation of PPO in the organic phase, in comparison with PEO. Moreover, enthalpy values for partitioning with chlorobenzene and dichloromethane are essentially the same, slightly more positive than those determined with chloroform. Once more, this indicates that specific interaction between organic solvents and PPO, which should involve hydrogen bonding, should not be so relevant for this process, because chlorobenzene behaves similarly to chloroform and dichloromethane.

Due to their limited solubility, calorimetric data could not be collected for PPO above $1000\,\mathrm{g\,mol^{-1}}$. Assuming that enthalpy values would remain constant above this molar mass, as they did with PEO after the point where end group contributions vanished, one can estimate a difference in the transfer enthalpy of EO and PO units of between *ca.* 3.5 and $5.5\,\mathrm{kJ\,mol^{-1}}$. Once more, assuming the same additivity scheme applied to analyze the Gibbs transfer energies (discussed above), this difference could be ascribed to the contribution from a methylene unit. Literature data are scarce for this parameter but, for comparison, one may use a report by Beezer *et al.*[9] that mentions a null enthalpic contribution from (CH_2) to the partitioning of a homologous series of alkoxyphenols between water and heptane or octanol.

By using the values of the Gibbs transfer functions and enthalpies, the entropies of transfer of PPO between the two phases can be calculated, as shown in Fig. 3. Again, the trend is similar to that observed for PEO, but with more positive entropic contributions. Assuming that a plateau is reached above PPO 1000, the difference between the transfer entropies of PEO and PPO, expressed as $T\Delta S$, can be estimated as *ca.* $6\,\mathrm{kJ\,mol^{-1}}$. Once more, for comparison, data for the (CH_2) contribution to the transfer entropy reported by Beezer et al.[9] vary between 3 and $4\,\mathrm{kJ\,mol^{-1}}$.

This more positive transfer entropy is in agreement with the frame of the hydrophobic effect, which proposes that water molecules restricted due to the presence of an apolar moiety in an aqueous phase are released upon its removal (in this case, transfer to the organic phase).

To further investigate this hypothesis, we determined the amount of water that is transferred with PPO to the different organic phases, obtaining the values listed in Table 1. These data were calculated using the amount of water determined in the organic phase in the presence and absence of PPO, relating the difference (moles of extra water present in the organic phase) to the amount of PO units in the organic phase. It is interesting to note that values for the number of moles of water solvating each PO unit is higher for the smaller PPO (425, 725, and 1000), decreasing with its molar mass until a constant value of *ca.* 0.02 moles of water per mole of PO unit. The same trend was observed for PEO,[6] and agrees with the proposition of different contributions from the hydroxyl end groups and monomer units in both cases. Moreover, constant ($n\mathrm{H_2O}/n\mathrm{PO}$) values are attained above molar masses that are consistent with the region for the transition between polyglycol to polyether behavior of PPO as determined from its Gibbs transfer energies and enthalpies (Figs. 1 and 2).

These data can be analyzed using an additivity scheme that assumes a fixed number of moles of water solvating the —OH and EO units, as previously applied to the partitioning of PEO.[6] Using this scheme, the plateau

Table 1. Water-dragging effect accompanying poly(propylene oxide) transfer from aqueous to organic phases

Polymer	Amount of water in the $CHCl_3$ phase (wt%)	(nH_2O/nPO)[a]	Amount of water in the CH_2Cl_2 phase (wt%)	(nH_2O/nPO)[a]	Amount of water in the C_6H_5Cl phase (wt%)	(nH_2O/nPO)[a]
No polymer	0.18 ± 0.04		0.16 ± 0.01		0.08 ± 0.01	
PPO 425	0.392 ± 0.007	0.052 ± 0.003	0.28 ± 0.02	0.03 ± 0.01	0.590 ± 0.002	0.11 ± 0.01
PPO 725	0.44 ± 0.01	0.051 ± 0.003	0.283 ± 0.006	0.02 ± 0.01	0.480 ± 0.002	0.09 ± 0.02
PPO 1000	0.357 ± 0.002	0.04 ± 0.01	0.264 ± 0.003	0.018 ± 0.007	0.440 ± 0.001	0.08 ± 0.01
PPO 2000	0.307 ± 0.004	0.02 ± 0.01	0.232 ± 0.003	0.007 ± 0.001	0.47 ± 0.002	0.07 ± 0.02
PPO 2700	0.326 ± 0.004	0.02 ± 0.02	0.21 ± 0.01	0.006 ± 0.002	0.48 ± 0.01	0.08 ± 0.01

[a] Values determined by subtracting the amount of water in the organic phase with and without polymer, then calculating the ratio between the number of moles of extra water molecules per PO unit in the organic phase.

values of *ca*. 0.02, 0.007, and 0.08 moles of water per mole of PO unit, respectively, in chloroform, dichloromethane, and chlorobenzene should remain constant for the smaller PPO, leading to values of 0.08 moles of water per mole of hydroxyl groups, in all of the three solvents. These values are lower than those determined for PEO:[6] 0.08 moles of water per EO unit (in chloroform and dichloromethane), and 0.3 and 0.6 moles of water per hydroxyl group, respectively, in chloroform and dichloromethane. The large difference between water molecules that remain solvating the PO units in the organic phase, with respect to EO units, may be related to the greater (and positive) entropic contribution to the transfer of PO from aqueous to organic phases. Interestingly, the number of water molecules that remain solvating the hydroxyl end groups of PPO is also smaller than for PEO, which may suggest that the assumption of an additivity scheme may not be completely correct, though valid as an estimate. Comparing these results with the current views on the partitioning of hydrophobic solutes, a large and positive transfer entropy is expected in line with the proposition of a hydrophobic effect. Once more, it is the trend observed for the partitioning of PEO that seems peculiar.

Partitioning of poly(vinyl pyrrolidone) and poly(acrylamide)

In order to investigate the partitioning of more hydrophilic polymers, PVP and PAM were investigated. With both PVP 10 000 and 55 000, partition coefficients of *ca*. 5×10^{-4} (corresponding to a Gibbs transfer energy of $14\,kJ\,mol^{-1}$) were determined with each of the three solvents. Similar values were determined for poly(acrylamide), confirming that these polymers reside almost quantitatively in the aqueous phases, in agreement with their hydrophilic character. For PVP 10 000 and 55 000, in systems with chloroform, transfer enthalpy values of *ca*. $6\,kJ\,mol^{-1}$ were determined, which are more positive than those for PEO, and similar to those measured for PPO. Using these values, a transfer entropy of $-8\,kJ\,mol^{-1}$ was calculated, in contrast with the positive values determined for PEO and PPO. Assuming the hypothesis that this entropy is related to the release of water molecules solvating the polymer, this may be interpreted as an indication of the incapacity of the organic solvents to displace water from the polymer solvation shell. Alternatively, it is also possible that the restriction of water molecules due to solvation of PVP is not as great as that caused by PEO, which is related to a close fit of PEO into the structure of liquid water, or by PPO, which is ascribed to hydrophobic restriction. Neither the transfer enthalpy nor the transfer entropy favor the partitioning of PVP to the organic phase, a feature that seems to fit better an assumption of a hydrophilic polymer.

CONCLUSIONS

This investigation confirmed that the thermodynamic transfer functions for PEO between aqueous and organic phases vary with its molar mass as a function of the contribution of its hydroxyl end groups, reaching a plateau value above *ca*. $2000\,g\,mol^{-1}$.

Partitioning of PPO showed the same behavior, except that the end group contributions vanish at lower molar mass, *ca*. $1000\,g\,mol^{-1}$. PPO is effectively extracted to all three chlorinated solvents, but for PEO this was not the case with chlorobenzene. Its partitioning to organic phases is followed by increases in enthalpy and entropy, both greater than the respective values measured for PEO. Much smaller amounts of water molecules were found to accompany the transfer of PPO to the organic phases, which may indicate a more extensive release of water molecules restricted around this polymer when in the aqueous phase, which could be the cause of this larger entropy increase. This

picture agrees well with that proposed as the basis of the hydrophobic effect.

On the other hand, partitioning of two other hydrophilic polymers, PVP and PAM, towards the aqueous phases, is prevalent. For PVP, this partitioning is accompanied by an increase in enthalpy similar to that determined with PPO, but associated with a significant decrease in entropy. Again, this behavior agrees with that predicted for hydrophilic polymers, stressing the peculiar partitioning behavior of PEO.

In summary, this investigation confirmed that hydrophilic polymers such as PVP and PAM stay preferentially in the aqueous phases, whereas a more hydrophobic polymer, PPO, is extracted to the organic phases. PEO, however, remains as an outlier to such a trend: it is undoubtedly hydrophilic, as confirmed by its total miscibility with water, but, due to an entropy increase, it may be quantitatively extracted to organic solvents that are capable of interacting as hydrogen bond donors, such as dichloromethane and chloroform. This duality, which has been referred to as 'the two faces of PEO,'[2] also appears in a variety of phenomena and it is hoped that this series of investigations may contribute to the understanding of this elusive behavior.

Acknowledgements

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