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Short Communication

Separation of polypropylene glycol 1200 and polybutylene glycol 1000 by reversed-phase high-performance liquid chromatography on a C_{18} stationary phase with different organic modifiers and detection by evaporative light scattering

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ABSTRACT

The separation of polypropylene glycol 1200 (PPG 1200) and polybutylene glycol 1000 (PBG 1000) was investigated by reversed-phase high-performance liquid chromatography on octadecylsilyl silica gel (C_{18}) with aprotic (acetonitrile) and protic (methanol, ethanol, 2-propanol) organic modifiers. Detector responses were monitored by means of evaporative light scattering. It was shown that the retentions of all oligomers of PPG 1200 decrease in the order methanol > acetonitrile > ethanol > 2-propanol. A biphasic elution pattern was observed with the more hydrophobic PBG 1000 and the retentions of low-molecular-mass homologues decreased in the order methanol > ethanol > acetonitrile > 2-propanol, whereas those of medium- and high-molecular-mass oligomers decreased in the order acetonitrile ≫ methanol > ethanol > 2-propanol. Participation of substantial solvophobic solute–solvent influences was hypothesized but the different mobile phase effects of the protic modifiers may also need to be taken into account. The former effect may be explained by interactions between the alkyl chains of ethanol and 2-propanol with the hydrophobic tetramethylene backbone of PBG 1000, which further enhances the solubility increase elicited by hydrogen bond formation between the hydroxyl groups of the organic solvent and the ether oxygens of the analyte. The latter effect may particularly be assumed in the case of methanol, where the methyl group seems to be too small to undergo efficient hydrophobic interactions with non-polar sites of the analyte.

INTRODUCTION

Polyethers and their α,ω-O-alkylated or arylated derivatives have a broad application range in many different fields of chemistry. In particular, polyethylene glycol (PEG) plays a major role in both industrial and biotechnical applications, whereas polypropylene glycol (PPG) and polybutylene glycol (PBG) play an important role in polymer chemistry as flexibilizers and toughenners in formulated systems [1–3]. In many applications PPGs are first reacted with diisocyanates to form isocyanate prepolymers, which are subsequently converted into polyurethanes [4,5].

Different chromatographic methods have been successfully used for the characterization of

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polyether mixtures, *e.g.*, gas chromatography (GC), gel permeation chromatography/size-exclusion chromatography (GPC/SEC), thin-layer chromatography (TLC), reversed-phase high-performance liquid chromatography (RP-HPLC) and supercritical fluid chromatography (SFC). GC yields an optimum resolution of polyethers but unfortunately its use is restricted to low-molecular-mass samples, whereas GC/SEC covers the whole molecular mass range but is associated with poor peak resolution. TLC can be used at least up to the intermediate molecular mass range but exhibits substantially less resolution in comparison with HPLC. SFC is a very promising new technique, but it is still restricted to a small number of suitable mobile phases. Therefore, HPLC may still be regarded as the most efficient technique for the separation of polyethers owing to the large number of experimental alternatives, *i.e.*, the wide availability of both mobile and stationary phases. Additionally, in combination with evaporative light scattering detection (ELSD), the monitoring of UV-inactive components is achieved with high sensitivity.

It should be taken into account that polyethers of technical quality generally consist of a large number of oligomers often yielding a distinct chromatographic pattern, which, in turn, can be used to identify the type of polyether within a formulated system by its "fingerprint".

In a previous paper, we treated the separation of polyethers, such as PEG 1000, PPG 1200 and PBG 1000, on different stationary phases with either acetonitrile or methanol as mobile phase modifier [6]. Methanol proved to be superior to acetonitrile especially for the elution of medium- to high-molecular-mass oligomers [6]. Its marked improvement of the elution power was attributed to solute solvation by hydrogen bonding with polyether oxygens and, as a consequence, retention seems to be essentially governed by its hydrophilic properties. The question arises of whether a "solvophobic solvation" effect of the alcoholic modifier on solute retention (*i.e.*, depending on the length of the alkyl chain and thus attributable to an increase in lipophilicity in the order methanol < ethanol < 2-propanol) will be synergistic with the effect of hydrogen bonding. On the other hand, mobile phase effects influencing desorption of the solute as a function of increasing elution strength in the order methanol < ethanol < 2-propanol has additionally to be considered. For this reason we have applied gradient RP-HPLC with PPG 1200 and PBG 1000 as model components on octadecylsilyl silica gel (C_{18}) with methanol, ethanol and 2-propanol as organic modifiers. Acetonitrile is used as a "reference" solvent, because it is not able to release medium- to high-molecular-mass homologues from the hydrophobic stationary phase, as shown recently [6].

EXPERIMENTAL

Reagents and solvents

Polypropylene glycol 1200 ("pract." quality) was purchased from Fluka (Buchs, Switzerland) and polybutylene glycol 1000 (technical quality) from BASF (Ludwigshafen, Germany). Acetonitrile, methanol and 2-propanol (all of HPLC quality) were from Fluka and ethanol was purchased from Merck (Darmstadt, Germany). Water for use in HPLC was purified with a Milli-Q reagent water system from Millipore–Waters (Milford, MA, USA).

Analytical equipment

The HPLC apparatus consisted of a combined-type SP 8100 system of an HPLC pump and autosampler and a PC 1000 data acquisition unit, all obtained from Spectra-Physics (San Jose, CA, USA). For ELSD a Sedex 45 apparatus from Sedere (Vitry sur Seine, France) equipped with a 20-W iodine lamp was used.

Chromatographic separation and detection

Separation of polyethers was performed on a Nucleosil $5C_{18}$ column (125 × 4.6 mm I.D., 5 μm particle size) from Macherey–Nagel (Oensingen, Switzerland). The gradient profile used is shown in Table I and chromatography was performed at ambient temperature (*ca.* 22°C) at a flow-rate of 1.5 ml/min. Polyether samples (2%, w/v) were dissolved in methanol and 10-μl aliquots were injected. For detection by means of ELSD the nebulization chamber was heated to 40°C and the nitrogen flow-rate was adjusted

TABLE I

GRADIENT PROGRAMME FOR THE ELUTION OF POLYETHER SAMPLES

Time (min)	Organic solvent (%)	Water (%)
0	20	80
40	100	0
75	100	0
76	20	80
90	20	80

to 4.5 l/min, corresponding to an inlet pressure of 200 kPa.

RESULTS AND DISCUSSION

On the basis of our experience in polyether analysis as described recently [6], we used signal monitoring by ELSD. Alternatively, tagging of a chromophoric agent to the α,ω-dihydroxy groups will permit UV detection in the usual wavelength range [7]. However, the increase in hydrophobicity of both polyethers through derivatization makes long elution times necessary, especially for PBG 1000.

The retention of PPG 1200 (a polyether of intermediate polarity) decreases substantially in the order methanol > acetonitrile > ethanol > 2-propanol (Fig. 1a–d). When compared with the peak resolution R_s obtained with acetonitrile (Fig. 1a), a significant "levelling" effect is observed with the protic solvents, resulting in fairly poor R_s values (Fig. 1b–d). With methanol the marked time delay in the onset of oligomer elution and the concomitant "compression" of peaks attributable to high-molecular-mass constituents to within a period of a few minutes when compared with acetonitrile can be explained by its decreased elution power for the low-molecular-mass homologues and to a concomitant relative increase in desorption of oligomers of higher molecular mass, presumably owing to their better solubility in the mobile phase by means of hydrogen bond formation between the hydroxy groups and polyether oxygens [6]. The further decrease in solute retention with ethanol and 2-propanol compared with methanol may be attributed to (i) stronger desorption as a consequence of a more efficient displacement of solute from the non-polar stationary phase by the more hydrophobic modifiers and/or (ii) an effect of "hydrocarbon (tetramethylene) backbone solvation" mediated by the alkyl groups of ethanol and 2-propanol, *i.e.*, a solvophobic solute–solvent effect.

In general, separation of the more hydrophobic PBG 1000 yields similar retention characteristics (Fig. 2a–d). Nevertheless, some peculiarities with respect to PPG 1200 are observed. The elution power of acetonitrile seems at first sight to be superior to that of methanol and ethanol, but it is evident that only a minor part of PBG 1000 oligomers was eluted on a C_{18} matrix. Therefore, the aprotic solvent proves to be the eluent of choice at least for the low-molecular-mass PBGs yielding optimum resolution of homologues. With methanol, more than twice the number of well resolved oligomers are eluted compared with acetonitrile but the complete release of the total amount of sample is only effected with ethanol and 2-propanol (Fig. 2c and d). In contrast, only oligomers with apparently low and medium molecular mass are well resolved by the use of ethanol and 2-propanol. It is conspicuous that a substantial discrimination between oligomers with different molecular mass takes place in particular at the change from methanol to ethanol and 2-propanol (see Fig. 2b–d). Further, retention of low-molecular-mass oligomers seems to be differently affected with ethanol and 2-propanol (Fig. 2c and d). This observation can be ascribed to a heterogenous distribution of oligomers in the PBG 1000 sample. We cannot give a reasonable explanation of these surprising mobile phase influences. Nevertheless a possible influence of the column pressure on retention and selectivity [8–11] of PBG 1000 with 2-propanol as the modifier may probably be ruled out. This view is supported by the observation that a consecutive temperature increase in 10°C intervals from room temperature to 70°C did neither essentially influence retention of oligomers nor the chromatographic pattern (results not shown).

Replacement of acetonitrile with methanol (Fig. 2b) effects a stronger retention of low-molecular-mass homologues, whereas sample

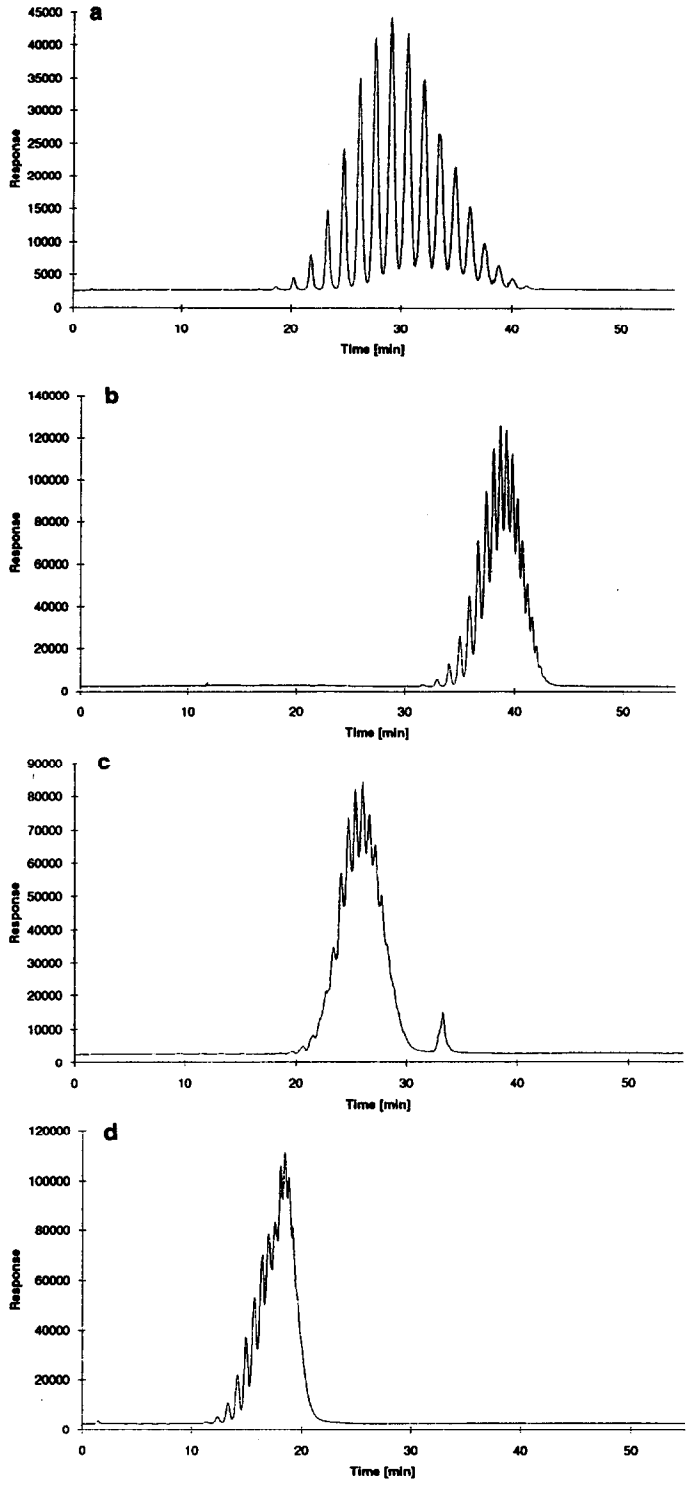

Fig. 1. HPLC of PBG 1000 on a C_{18} column with (a) acetonitrile, (b) methanol, (c) ethanol and (d) 2-propanol as the organic modifier.

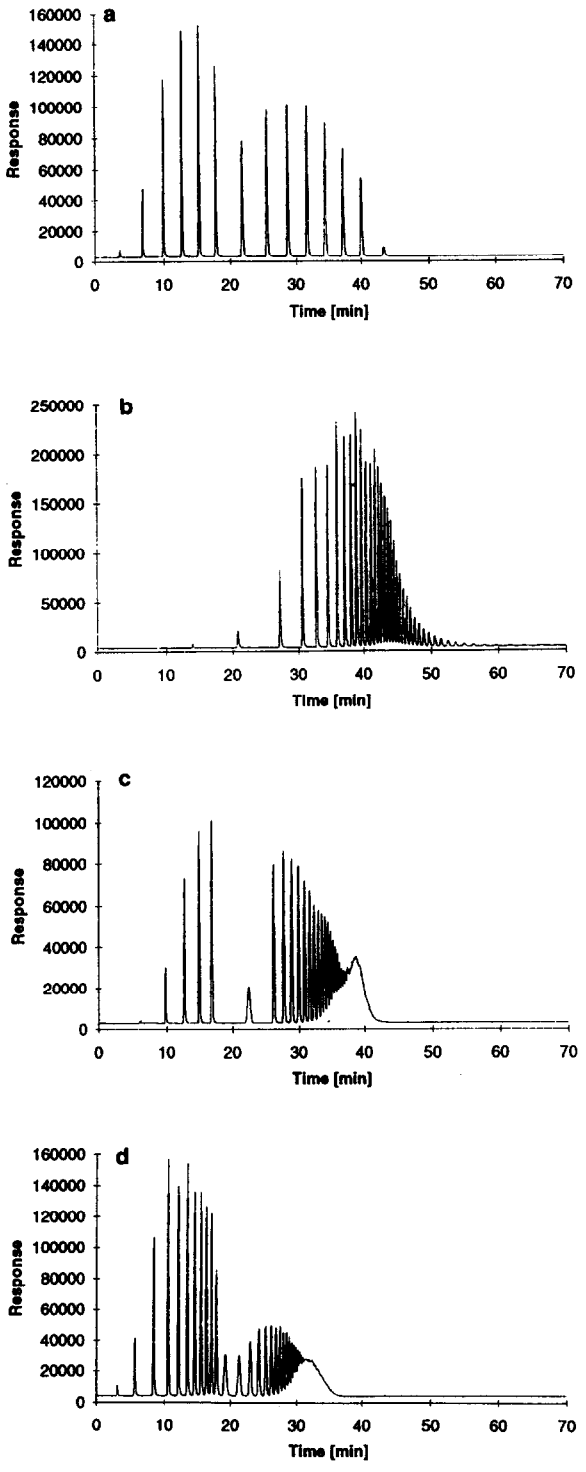

Fig. 2. HPLC of PBG 1000 on a C_{18} column with (a) acetonitrile, (b) methanol, (c) ethanol and (d) 2-propanol as the organic modifier.

constituents of higher mass are eluted either more rapidly or more quantitatively (see ref. 6). It may be assumed that low-molecular-mass oligomers are sufficiently soluble in acetonitrile and, owing to its superior elution power, are eluted more rapidly than with methanol and ethanol. Although more than twice the number of oligomers are released with methanol, its beneficial effect on the solubility of PBG 1000, at least on a C_{18} column, is not sufficient enough for their quantitative elution. Concerning the large increase in elution power elicited by ethanol, we suggest a substantial participation of solvophobic (*i.e.*, solubility-enhancing) interactions between the lipophilic side-chain of ethanol and 2-propanol ($+CH_2-$ and $+CH_3CH-$ *versus* methanol) in the order 2-propanol > ethanol > methanol and the hydrophobic tetramethylene backbone of PBG 1000, which, in turn, may be responsible for the increase in desorption. This hypothetical view is supported by the fact that the retention of high-molecular-mass components (eluting at high concentrations of the modifier) is obviously much more affected than that of low-molecular-mass sample constituents and yields substantial "signal compression" (Fig. 2c and d). It may be assumed that low-molecular-mass oligomers, their solubilities being approximately identical in all four organic solvents, are less affected and elute nearly in the range of the modifier's elution power. Nevertheless a contribution of a mobile phase effect to retention should also be considered. This means that the increase in elution power in the order methanol < ethanol < 2-propanol (*i.e.*, depending on the modifier's hydrophobicity) may be ascribed to the better sorption of the alcohols on the stationary phase and thus increased desorption of the analyte in the same direction. However, the large discrepancies in retention between methanol and ethanol may be interpreted as supporting our hypothesis. This point of view is further corroborated by (i) the strongly increasing "signal compression" of high- compared with low-molecular-mass PBG 1000 oligomers in the order methanol < ethanol < 2-propanol and (ii) the different effects of ethanol and 2-propanol on the retention of low- and medium-molecular-mass oligomers compared with metha-

nol, which cannot be explained by stronger desorption alone. In this respect we hypothesize an additional solvophobic solute–solvent interaction in addition to also a reasonably substantial "mobile phase" influence mentioned above, which superimposes the effect of hydrogen bond formation. As an appropriate means of obtaining a more quantitative estimate of the extent of solovophobic solute–solvent interactions compared with a "mobile phase" effect based on increased desorption from the stationary phase, measurement of the heats of solubility of both analytes in the different modifiers would be feasible.

According to our previous investigations with different stationary phases [6], silanophilic solute–matrix interactions [12–15] do not seem to play a significant role. Hence the elution power of the protic solvents *versus* acetonitrile probably cannot be attributed to their better ability to cleave hydrogen bonds between polyether oxygens and residual silanols of the stationary phase [12].

It will further be of interest if the trend observed within the series of C_1, C_2 and C_3 alcohols continues with butanol. However, the expected back-pressure of the HPLC column will prevent its use at least at room temperature. It is notable that the column back-pressure of aqueous solutions of the three alcoholic modifiers reaches a maximum value at *ca.* 40–70% (v/v) of organic solvent (depending on the modifier used), which with 2-propanol markedly exceeds 300 bar. For this reason, at least for C_4 alcohols, column heating is necessary and thus micro-HPLC at elevated temperature will offer an attractive alternative for the use of alcohols with more than four carbon atoms and alcohols of the ethylene glycol or diethylene glycol type. In addition, it may be of great importance to evaluate the possible influence of column temperature on the retention of hydrophobic polyethers, by means of which more insight into the separation mechanism should be possible. This aim will only be achieved, however, by testing more than three homologous alcohols as used in our study, which, in turn, also raises the question of sufficient miscibility of, *e.g.*, C_4–C_6 alcohols and water even at elevated temperature.

CONCLUSIONS

From the chromatograms in Figs. 1a–d and 2a–d, it can be concluded that the separation efficiency of oligomers on the C_{18} matrix is substantially higher for PBG 1000 than PPG 1200, which, as a consequence, facilitates identification of PBG 1000 by the "fingerprint" pattern of its low- and medium-molecular-mass oligomers. This "pattern recognition" is even possible with the stronger modifiers ethanol and 2-propanol, which, however, do not or at least insufficiently resolve high-molecular-mass homologues. Although the R_s of PPG 1200 oligomers vanishes completely with both ethanol and 2-propanol it should be emphasized that discrimination of different PPG samples ranging from $M_r = 2000$ to more than 10 000 is still possible and allows a selective attribution within polyether mixtures compared with GPC (preliminary investigations, results not shown).

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