Reactive polymers: 61. Reaction of macroporous poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) with phenol

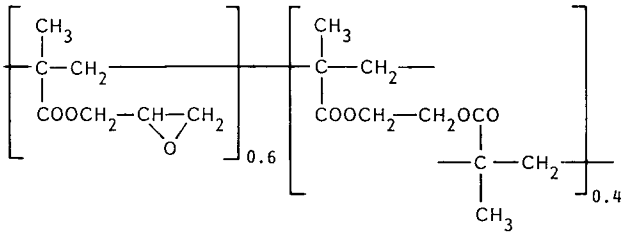
D. Horák, J. Straka, J. Štokr, B. Schneider, T. B. Tennikova*
and F. Švec†
Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences,
162 06 Prague 6, Czechoslovakia
(*Received 18 October 1989; revised 20 February 1990; accepted 4 June 1990*)

A series of sorbents differing substantially in the content of phenyl groups were prepared by a base-catalysed reaction of poly(glycidyl methacrylate-*co*-ethylene dimethacrylate) with phenol. Methods are described for quantitative determination of the degree of substitution of epoxide groups by phenol, based on ^{13}C nuclear magnetic resonance and infra-red spectroscopy and on elemental analysis (C, H); the last method was found to be inappropriate, however, owing to the large error involved. Infra-red spectroscopy is the method of choice for determining the degree of substitution. By studying the local properties of the regression surface, a polynomial equation was derived for the dependence of the degree of substitution of epoxide groups by phenol on the mole ratios phenol/epoxide and sodium hydroxide/phenol. The time dependence of the extent of reaction was also studied. The maximum degree of substitution attained was 0.65.

(Keywords: glycidyl methacrylate; ethylene dimethacrylate; infra-red spectroscopy; ^{13}C nuclear magnetic resonance spectroscopy)

INTRODUCTION

Since their discovery in the mid-1970s[1], macroporous glycidyl methacrylate/ethylene dimethacrylate (GMA-EDMA) copolymers with the structure shown below have found many applications in such diverse fields as sorption of metal ions[2], enzyme immobilization[3], phase-transfer catalysis[4] and gas chromatography[5]:



GMA - EDMA (60:40)

Recently they have also been found to be applicable to high-performance liquid chromatography (h.p.l.c.) in both the size-exclusion[6,7] and adsorption modes[8]. In the latter case, ion-exchange h.p.l.c. and partly also hydrophobic interaction h.p.l.c. (h.i.c.)[8] were tested with sorbents having their surface modified by aliphatic alcohols with four or eight carbon atoms. As h.i.c. ranks among the most important methods for the separation of proteins[9], it would be advisable to have at one's disposal a series of sorbents differing in the polarity of the hybrid (hydrophilic/hydrophobic) support to cover a whole spectrum of finely tuned processes for the separation of complex mixtures.

In comparison with other polymeric supports used in h.i.c., such as 2-hydroxyethyl methacrylate (HEMA)/EDMA copolymers (Separon HEMA, Tessek, Czechoslovakia; Toyopearl, Tosoh Corp., Japan), GMA-EDMA copolymers offer the advantage of sufficiently high chemical reactivity, due to the presence of epoxide groups. Many reactions with various compounds, including ammonia and amines[10], strong acids[11], or concentrated bases[12], have already been described; products of these reactions can also be used in ion-exchange chromatography. Reaction of the GMA-EDMA copolymer with phenol has not been studied yet; in view of the possibility to use the reaction product in h.i.c., we describe in this study reaction conditions and methods for controlling the content of phenyl groups in the reaction product, along with some tested procedures for their quantitative determination.

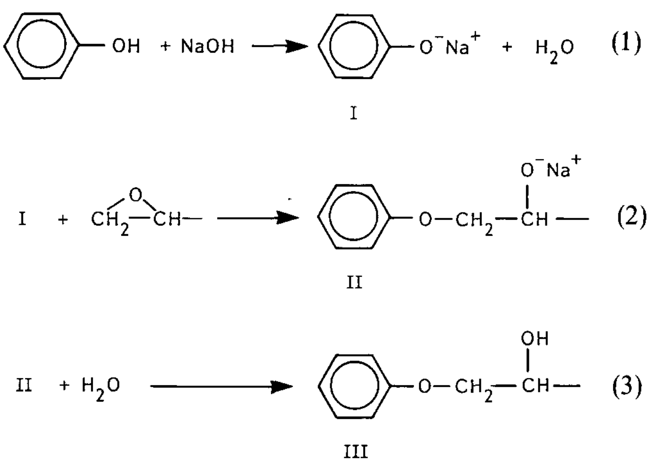
In the investigation we were guided by experience related to the synthesis of epoxide resins from 4,4′-isopropylidenebisphenol (bisphenol A) and bisglycidyl ethers[13]. Reaction mechanisms have been described for reactions catalysed by acids or bases, although the latter have found much broader application. Under such conditions the addition of phenol is much more rapid than that of water or of alcohols; these compounds therefore do not interfere and no elaborate measures are necessary to remove them from the reaction mixture. In the first step phenol reacts with the alkali hydroxide to yield salt I, which is then added onto the epoxide group to form an ether bond and alcoholate group II; the latter

---

* On leave from the Institute of Macromolecular Compounds, Academy of Sciences of the USSR, Leningrad 199004, USSR
† To whom correspondence should be addressed

0032-3861/91/061135-05

immediately reacts with water present in the reaction mixture and yields the final product III:



EXPERIMENTAL

Compounds

Macroporous GMA-EDMA copolymer (60:40) was prepared by suspension radical polymerization in the presence of cyclohexanol and 1-dodecanol as porogens[14]. A single copolymer with particle size 10–16 μm, specific surface area 68.5 $m^2\,g^{-1}$, most frequent pore radius 30 nm and porosity ~60% was used throughout this study. Phenol was distilled prior to the reaction. Dioxane used as the reaction medium was dried by boiling over sodium metal and distilled. The remaining compounds (of p.a. purity) were used as received.

Methods

Although the reaction conditions were varied during the study, the following was a typical experimental procedure. First 2.5 g of NaOH (63 mmol) and 11.9 g of phenol (126 mmol) were dissolved under stirring in 40 ml of dioxane heated to about 80°C. Then 1 g of the GMA-EDMA copolymer (theoretical content of epoxide groups 4.22 mmol) was added and the suspension was stirred for 2 h at 80°C. The product was separated by filtration on a fritted glass, packed into a column, washed with water until neutral, and then in turn with methanol, acetone and diethyl ether, and finally dried *in vacuo*.

To limit the number of experiments to the absolute minimum, an orthogonal factorial experimental design was employed; the results were evaluated by the methods of mathematical statistics to yield the regression surface and the pair correlation coefficient characterizing the closeness of fit between pairs of variates[15].

The degree of substitution of epoxide groups by phenol (conversion) was evaluated from ^{13}C cross-polarization/magic-angle spinning (CP/MAS) n.m.r. spectra, from i.r. spectra and from the results of elemental analysis (C, H).

CP/MAS n.m.r. spectra of solid samples were registered on a Bruker MSL 200 spectrometer at room temperature[16–18], with 90° pulses of 5–6 μs duration, contact time 3 ms, pulse repetition time 3 s, MAS frequency 4.5 kHz, spectral width 20 kHz, acquisition time 26 ms and number of transients 2400. Samples were measured in double-bearing aluminium oxide rotors provided by the Bruker Co. Chemical shifts refer to the signal of carbonyl carbon in glycine ($\delta = 176.0$ ppm).

I.r. spectra (KBr pellets) were registered on a Perkin–Elmer 580 B spectrometer; a Perkin–Elmer CHN Elemental Analyser model 240 was used in the elemental analysis. The water regain in the pores as a measure of porosity was determined by means of the centrifugation method described elsewhere[19].

RESULTS AND DISCUSSION

It follows from the reaction mechanism presented in the 'Introduction' that the rate of reaction between phenol and the epoxide groups in GMA-EDMA copolymer will be influenced not only by the ratio of epoxide and phenol concentrations, by the similar ratio of phenol and hydroxide, by temperature and reaction time, i.e. standard variables relevant for all chemical reactions, but also by specific effects characteristic for reactions with participation of an insoluble polymer, such as particle size, pore diameter, degree of swelling, accessibility of reactive groups, rate of diffusion, etc. Since it would be difficult to optimize all these variables, any change in copolymer properties was excluded *a priori* and the same material was used throughout the study. Attention was focused on the first two parameters from the above list.

Determination of conversion in the reaction of phenol with the epoxide groups of the copolymer is a problem. Since no new atoms are introduced into the product as a result of the reaction, detection of new atoms cannot be used. Elemental analysis is a possibility, since the ratio of carbon and hydrogen atoms is changed by the reaction. Another feasible approach is spectroscopy. Finding a reliable method for the determination of conversion was therefore the first objective.

^{13}C CP/MAS n.m.r. spectroscopy

A typical spectrum of a GMA-EDMA copolymer reacted with phenol is shown in *Figure 1*. The signal of carbonyl carbon atoms centred at 176.8 ppm and the signal at 158.8 ppm of aromatic carbons in the phenyl group, directly bound to oxygen, can both be used for evaluating the degree of substitution. The results of quantitative evaluation of line intensity in CP/MAS spectra are known to depend on the contact time. Line intensity depends on the contact time as[20,21]:

$$I=\frac{I_0}{T_{\mathrm{CH}}}\left[\exp\left(-\frac{\tau}{T^{\mathrm{H}}_{1\rho}}\right)-\exp\left(-\frac{\tau}{T_{\mathrm{CH}}}\right)\right]\left(\frac{1}{T_{\mathrm{CH}}}-\frac{1}{T^{\mathrm{H}}_{1\rho}}\right)^{-1} \qquad (4)$$

provided $T^{\mathrm{C}}_{1\rho} > T^{\mathrm{H}}_{1\rho} \gg T_{\mathrm{CH}}$. The constants T_{CH} and $T^{\mathrm{H}}_{1\rho}$ may be in general different for different chemical groups in the investigated sample. To eliminate this effect, the

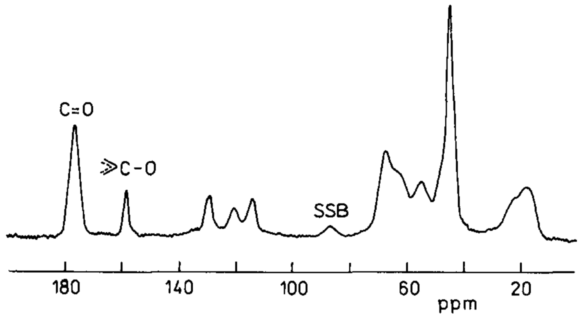


Figure 1 ^{13}C CP/MAS n.m.r. spectrum of GMA-EDMA copolymer reacted with phenol

Table 1 Effect of factors x_1 and x_2 on the degree of substitution[a] of epoxide groups by phenol

Polymer	x_1	x_2	A_{690}/A_{2940}	DS_{nmr}	DS_{ir}
1	5	0.1	0.311	0.21	0.180
2	5	0.55	0.598	0.31	0.345
3	5	1	0.541	0.27	0.313
4	17.5	0.1	0.572	0.30	0.330
5	17.5	0.55	0.720	0.41	0.416
6	17.5	1	0.594	0.37	0.343
7	30	0.1	0.592	0.33	0.342
8	30	0.55	0.804	0.49	0.464
9	30	1	0.617	0.40	0.356

[a] Degree of substitution determined by ^{13}C CP/MAS n.m.r. (DS_{nmr}) and by i.r. spectroscopy according to equation (6) (DS_{ir}); x_1 is the mole ratio phenol/epoxide groups, x_2 is the mole ratio NaOH/phenol

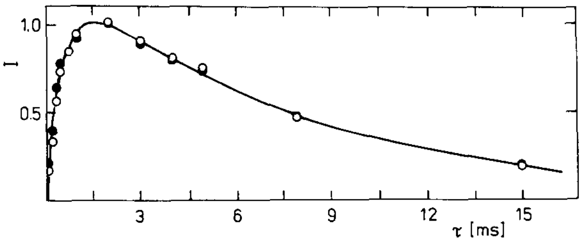


Figure 2 Dependences of band intensities on contact time for the carbonyl carbon band (○) and for the band of the aromatic carbon directly bound to oxygen (●). GMA-EDMA copolymer reacted with phenol; both dependences normalized to equal maximum intensity

line intensity was measured as a function of contact time for polymer 8 (*Table 1*). The dependences obtained for lines 176.8 and 158.8 ppm (both normalized to identical maximum intensity) are shown in *Figure 2*; the full curve is the least-squares fit according to equation (4). It is apparent from *Figure 2* that the dependence on contact time is the same for both lines and is described by the parameters $T_{CH} = 512\,\mu s$, $T^{H}_{1\rho} = 8.2\,ms$. The ratio of integrated intensities of the two lines is then independent of the contact time and can be used for quantitative evaluation. Spinning rate is another factor that can influence quantitative interpretation of CP/MAS spectra. If it is small in comparison with the width of chemical shift anisotropy, a noticeable part of the intensity is concentrated into the spinning sidebands (SSB). However, measurements with different rotor speeds have shown that, within the range of spinning frequency 2500 to 4500 Hz, the ratio of integrated intensities of the selected bands is independent of frequency and the effect of SSB can be neglected.

All products in this study were prepared from the same starting copolymer, for which the mole ratio of total carbonyls to epoxide groups was 2; since the integrated intensity of a n.m.r. signal is proportional to the amount of the corresponding group, the ratio of integrated intensities of bands centred at 176.8 and 158.8 ppm in a fully substituted sample will be also 2. The degree of substitution (DS_{nmr}) was therefore calculated from the formula:

$$DS_{nmr} = (I_B/I_A) \times 2 \qquad (5)$$

where I_A is the integrated intensity of the signal of carbonyl carbons and I_B is the intensity of the line corresponding to aromatic carbon atoms directly bound to oxygen. The reproducibility of the measurements was verified using polymer 8 (*Table 1*). Five measurements were evaluated and resulting standard deviation did not exceed 1%.

I.r. spectroscopy

The i.r. spectrum of a GMA-EDMA copolymer (copolymer 8) reacted with phenol is shown in *Figure 3*. It is apparent that during the base-catalysed reaction of GMA polymers with phenol the ester groups are not cleaved and no carboxylates or carboxyl groups are formed. Absorption bands centred at 690 and 2940 cm^{-1} were used for determining the content of phenyl groups in the studied samples. These two bands have comparable intensities and the mosaic effect will therefore influence the ratio of intensities relatively weakly[22]. Absorbances were measured at the band maxima; the selected baselines are apparent from *Figure 3*. The band at 690 cm^{-1} is characteristic for vibrations of a monosubstituted benzene ring; no band exists in this region in the spectrum of the original, non-reacted copolymer. The band at 2940 cm^{-1} belongs to valency vibrations of aliphatic CH bonds both in the parent copolymer and in the copolymer with attached phenyl groups. The number and character of aliphatic CH bonds is not affected by phenol substitution. One may also assume that the extinction coefficients of the band at 2940 cm^{-1} will be the same in the starting copolymer and in the product of its reaction with phenol. We checked the validity of this assumption by plotting the ratio of absorbances A_{690}/A_{2940} listed in *Table 1* against the degree of substitution of epoxide groups by phenol as determined from the n.m.r. spectra. Since the resulting dependence is linear and the straight line goes through the origin (*Figure 4*), it is apparent that the extinction coefficient of the band centred at 2940 cm^{-1} is indeed identical in the non-reacted and reacted copolymer. The degree of substitution then can be calculated from the formula:

$$DS_{ir} = k(A_{690}/A_{2940}) \qquad (6)$$

By linear regression applied to the dependence of the degree of substitution determined from n.m.r. spectra on the ratio A_{690}/A_{2940}, the constant k was found to be 0.58 and the standard error in k was 0.067 (*Table 1*). It must be noted that the above value of k is valid only for the copolymer used in this study, which contained 60% GMA and 40% EDMA. Values of DS_{ir} calculated from the above formula are listed in *Table 1*. On average, the differences between values of DS determined from the i.r. and n.m.r. spectra did not exceed 3%.

Repeated measurements (five replications) of i.r. spectra on identical samples have shown the intensities of bands at 690 and 2940 cm^{-1} to exhibit a standard error lower than 2% of the mean. Although the degree of substitution can be equally well determined from n.m.r. and i.r. spectra, all prepared samples were analysed only by i.r. spectroscopy since the necessary instrumentation is available in all laboratories and the procedure is quicker and cheaper than the measurement of ^{13}C CP/MAS spectra.

Effect of reaction conditions on the degree of substitution

To achieve proper control over the investigated process we sought the reaction conditions corresponding to the maximum conversion. An experimental region was first delimited on the basis of preliminary experiments;

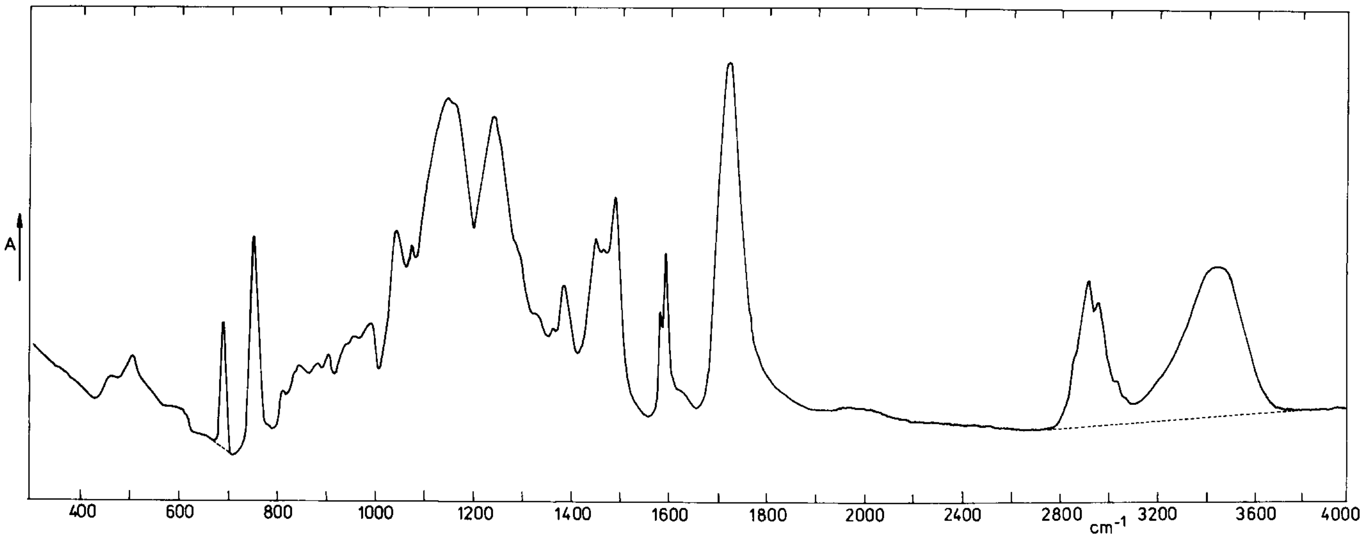


Figure 3 I.r. spectrum of GMA-EDMA copolymer reacted with phenol

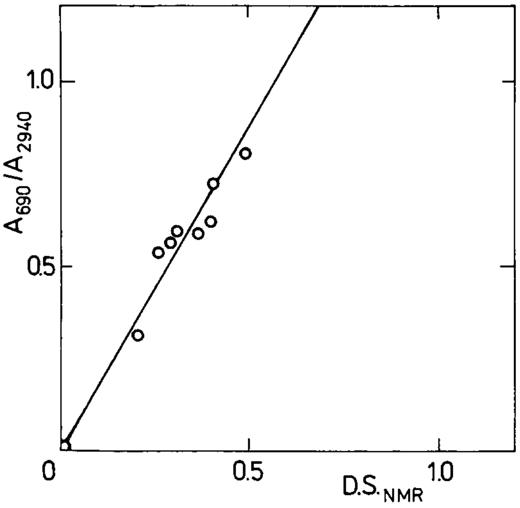


Figure 4 The ratio of absorbances of bands centred at 690 and 2940 cm^{-1} as a function of degree of substitution DS_{nmr}

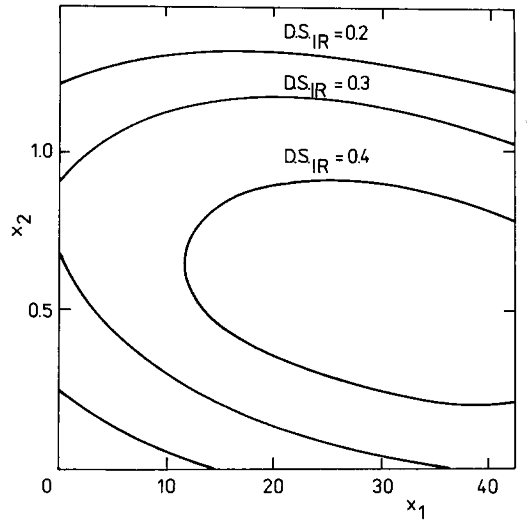


Figure 5 Regression surface plotted as the dependence of the degree of substitution on the mole ratio phenol/epoxide groups (x_1) and on the mole ratio NaOH/phenol (x_2); reaction time 2 h, 80°C

the character of the regression surface and the position of the maximum was then determined by varying the mole ratios phenol/epoxide groups (x_1) and sodium hydroxide/phenol (x_2). The experimental points were localized so as to enable the regression surface to be approximated by a second-degree polynomial. In a detailed analysis of the effects of x_1 and x_2 on the degree of substitution, coefficients of a second-order polynomial approximating the regression surface were estimated on the basis of a factorial experiment 3^2. New, transformed levels of the factors $(-1, 0, +1)$ were introduced to simplify the subsequent calculations. The resulting polynomial equation of the regression surface was:

$$DS_{\mathrm{ir}} = 0.4258 + 0.055x_1 + 0.027x_2 - 0.029x_1x_2 - 0.026x_1^2 - 0.097x_2^2 \tag{7}$$

The *F* criterion was used to check whether the above equation appropriately reflected the actual relationship between the variate and the predictors. *Figure 5* depicts the regression surface as contour curves of constant degree of substitution in the plane x_1, x_2. It is obvious that the regression surface has a single real maximum lying at the mole ratio phenol/epoxide groups = 30 and mole ratio NaOH/phenol = 0.5. It follows from the regression coefficients in equation (7) and from the shape of the regression surface that the degree of substitution rises with increasing mole ratio phenol/epoxide groups up to the value of 30 and with increasing mole ratio NaOH/phenol only up to 0.5. Equation (7) allows the degree of substitution to be predicted for any (transformed) pair x_1, x_2 inside the given experimental region.

The above experiments were carried out at a relatively short reaction time of 2 h to emphasize the effects of the factors x_1 and x_2. However, reaction time is very important for the degree of substitution and was followed next. Results for the case when the factors x_1 and x_2 lead to the optimum result according to equation (7) are shown in *Figure 6*, which provides evidence that the degree of substitution is practically independent of the reaction time only after 8 h. The maximum degree of substitution attained was 0.65.

Further investigation was devoted to the effect of water content on the chemical transformation of epoxide groups in GMA-EDMA copolymers reacted with phenol (*Figure 7*). Despite the scatter, probably due to hetero-

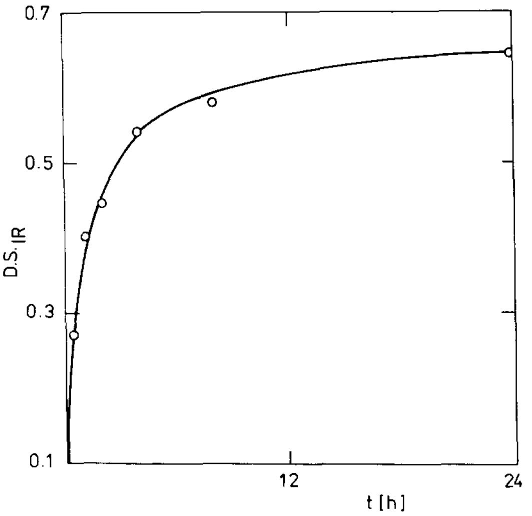


Figure 6 Time dependence of the degree of substitution DS_{ir}; reaction temperature 80°C, mole ratio phenol/epoxide groups = 30, mole ratio NaOH/phenol = 0.55

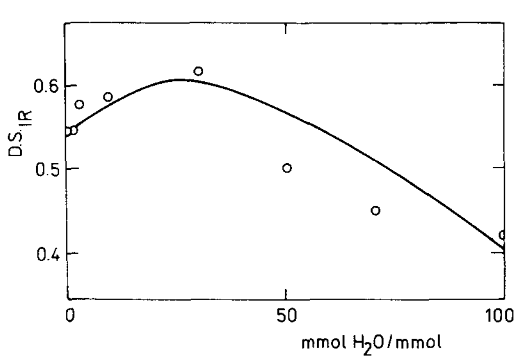


Figure 7 Degree of substitution DS_{ir} plotted against the amount of water added to the reaction mixture; reaction time 8 h, temperature 80°C, mole ratio phenol/epoxide groups = 30, mole ratio NaOH/phenol = 0.55

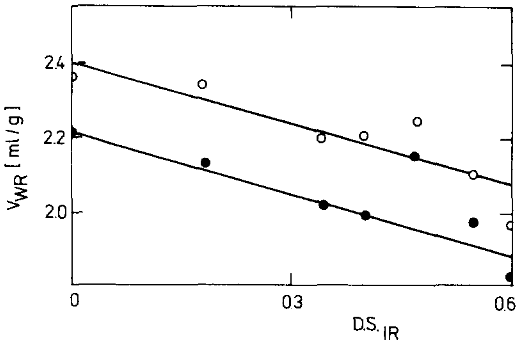


Figure 8 Effect of the degree of substitution DS_{ir} on the pore volume calculated from water regain after first swelling (○) and reswelling (●) of a dried copolymer

geneity of samples, it is apparent that the dependence goes through a weak maximum in the region of small contents of water and then begins to fall. Hence, it would be pointless to strive for anhydrous reaction conditions, a conclusion that agrees with literature data[23]; preparation of anhydrous phenol and NaOH would unnecessarily complicate the synthesis anyway.

Water regain as a function of the degree of substitution is shown in *Figure 8*. With increasing degree of substitution, the water regain decreases because the polymer matrix becomes more hydrophobic and therefore less attractive for water. In samples that have been dried and reswollen in water, the character of this dependence is preserved although the water regain is systematically lower by some 7%. This also agrees with literature data, which provide evidence that repeated drying and swelling of polymers leads to changes of porous structure and to a loss of porosity[24]. The macroporous structure of reswollen poly(phenyl-GMA-EDMA) samples was restored to 98%.

The reaction of GMA-EDMA copolymer with phenol also results in a certain change in specific surface area (68.5 $m^2 g^{-1}$ in the parent copolymer, 76.1 $m^2 g^{-1}$ in a copolymer with the degree of substitution $DS_{\mathrm{ir}} = 0.61$).

REFERENCES

1 Švec, F., Hradil, J., Čoupek, J. and Kálal, J. *Angew. Makromol. Chem.* 1975, **48**, 135

2 Švec, F., Kálalová, E., and Kálal, J. *Angew. Makromol. Chem.* 1985, **136**, 183

3 Drobník, J., Saudek, V., Švec, F., Kálal, J., Vojtíšek, V. and Bárta, M. *Biotech. Bioeng.* 1979, **21**, 1317

4 Hradil, J., Švec, F., Koňák, Č. and Jurek, K. *Reactive Polym.* 1988, **9**, 81

5 Lukáš, J., Švec, F. and Kálal, J. *J. Chromatogr.* 1978, **153**, 15

6 Tennikova, T. B., Horák, D., Švec, F., Kolář, J., Čoupek, J., Trushin, S. V., Maltzev, V. G. and Belenkii, B. G. *J. Chromatogr.* 1988, **435**, 357

7 Tennikova, T. B., Horák, D., Švec, F., Tennikov, M. B., Kever, E. E. and Belenkii, B. G. *J. Chromatogr.* 1989, **475**, 187

8 Tennikova, T. B., Náhunek, M., Švec, F., Almazova, T. V., Nasledov, D. G., Maltzev, V. G. and Belenkii, B. G. *J. Chromatogr.* in press

9 Mikeš, O. in 'High Performance Liquid Chromatography of Biopolymers and Biooligomers', Part B, Elsevier, Amsterdam, 1988, p. B26

10 Švec, F., Hrudková, H., Horák, D. and Kálal, J. *Angew. Makromol. Chem.* 1977, **63**, 23

11 Azanova, V. V., Hradil, J., Švec, F., Pelzbauer, Z. and Panarin, E. F. *Reactive Polym.* in press

12 Hradil, J. and Švec, F. *Reactive Polym.* 1985, **3**, 91

13 McAdams, L. V. and Gannon, J. A. in 'Encyclopedia of Polymer Science and Engineering', 2nd Edn (Ed. J. I. Kroschwitz), Wiley, New York, 1986, Vol. 6, p. 322

14 Horák, D., Pelzbauer, Z., Bleha, M., Ilavský, M., Švec, F. and Kálal, J. *J. Appl. Polym. Sci.* 1981, **26**, 411

15 Felix, M. and Bláha, K. in 'Methods of Mathematical Statistics in the Chemical Industry' (in Czech), SNTL, Prague, 1962

16 Schaefer, J., Stejskal, E. O. and Buchdahl, R. *Macromolecules* 1975, **8**, 291

17 Andrew, E. R. *Prog. Nucl. Magn. Reson. Spectrosc.* 1971, **8**, 1

18 Pines, A., Gibby, M. G. and Waugh, J. S. *J. Chem. Phys.* 1973, **59**, 589

19 Štamberg, J. and Ševčík, S. *Collect. Czech. Chem. Commun.* 1966, **31**, 1009

20 Mehring, M. 'Principles of High Resolution NMR in Solids', Springer, Berlin, 1983

21 Garroway, A. N., Moniz, M. B. and Resing, H. A. *ACS Symp. Ser.* 1979, **103**, 67

22 Jakeš, J., Slabina, K. and Schneider, B. *J. Appl. Spectrosc.* 1972, **26**, 389

23 Meerwein, H. 'Methoden zur Herstellung und Umwandlung von Äthern', in 'Methoden der Organischen Chemie' (Eds Houben and Weyl), Vol. VI/3, Vierte Auflage, Georg Thieme Verlag, Stuttgart, 1963, p. 79

24 Okay, O. *Angew. Makromol. Chem.* 1988, **157**, 15