CHROM. 3693

# MOLECULAR WEIGHT FRACTIONATION OF POLYETHYLENE GLYCOL BY GAS CHROMATOGRAPHY

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(Received June 3rd, 1968)

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## SUMMARY

The authors carried out temperature-programmed, gas chromatographic, molecular-weight fractionation of various derivatives of polyethylene glycol, with the general formulae $RO(CH_2CH_2O)_nR$ (R = Me, Ph, TMS) and $R(CH_2CH_2O)_n$-$CH_2CH_2R$ (R = Cl, PhS), in order to determine which derivative has the highest volatility and thermal stability and the lowest energy of adsorption on the support, thus making it the most suitable for the routine analysis of polyethylene glycol products with a molecular weight of less than 1000. Although the dimethyl derivatives are the most volatile, the bis-trimethylsilyl derivatives are the most suitable for the analysis of polyethylene glycol by GLC under the conditions used.

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## INTRODUCTION

Polyethylene glycols are important surfactants, and yet little work has been done to determine the distribution of the degree of polymerization. These compounds have the general formula $RO(CH_2CH_2O)_nR'$, where R and R′ denote *e.g.* hydrogen atoms, alkyl groups, or alkylaryl groups. Amongst the chromatographic techniques proposed for the analysis of surfactants (see ref. 1 for a bibliography), GLC is the most promising for the rapid determination of the distribution of the degree of polymerization since it entails the molecular weight fractionation of the products and the quantitative estimation of the resulting molecular-weight fractions by a suitable detector. With polyethylene glycol[2,3] and its monononylphenyl[4] and monoalkyl[5] ethers, however, low volatility restricts this analysis to the lower members. New possibilities were opened up by the discovery that the relative retention volume decreases as the two primary OH groups are successively substituted by methoxy groups[6]. The acetylation of the OH group has recently been suggested for the analysis of monoalkyl ethers[7], and has also been utilized in the analysis of polyglycerols[8], since the acetylated derivatives have a higher volatility and thermal stability.

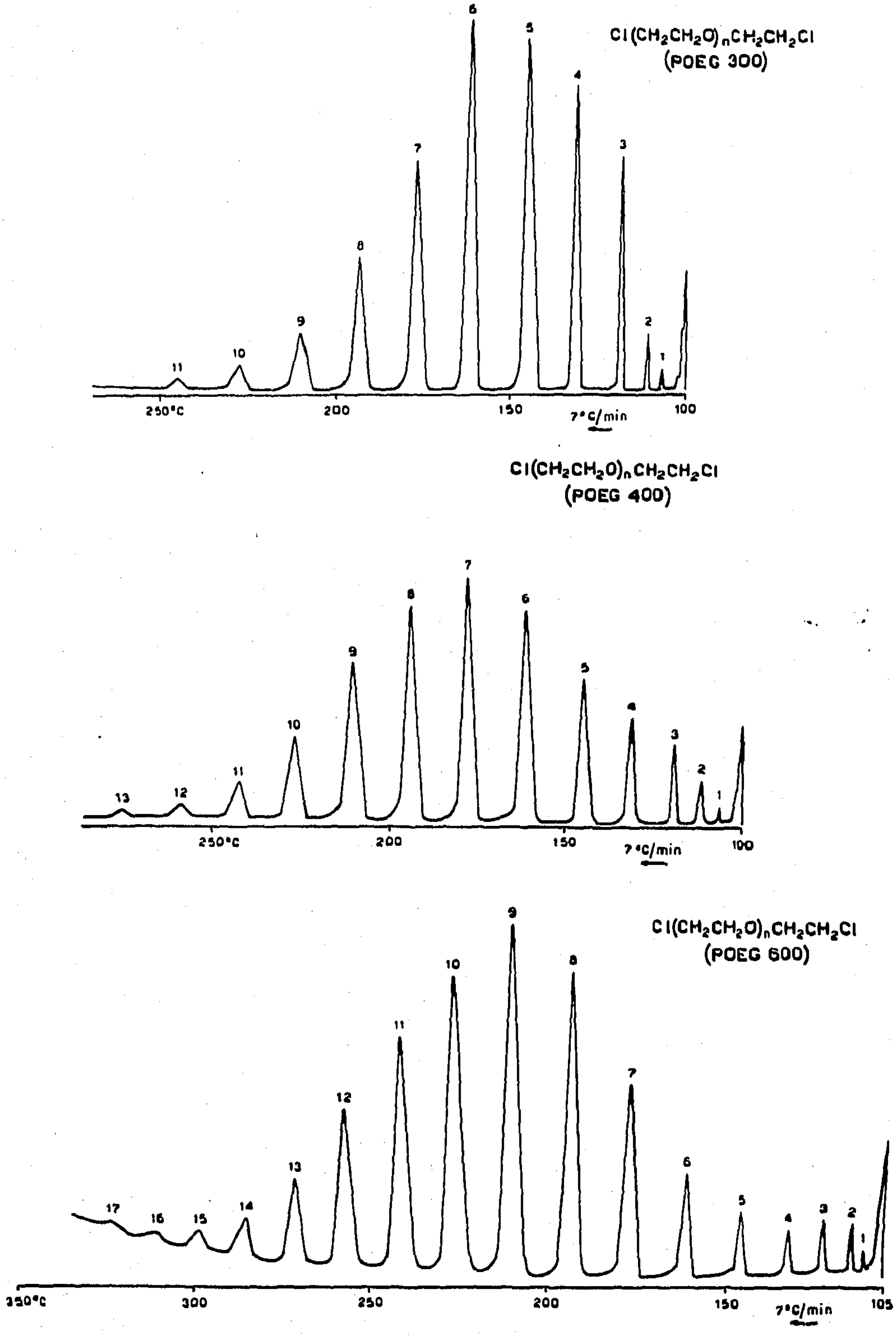

Cl(CH₂CH₂O)ₙCH₂CH₂Cl
(POEG 300)
6
5
4
7
3
8
9
2
10
11
1
250°C
200
150
7°C/min
100
Cl(CH₂CH₂O)ₙCH₂CH₂Cl
(POEG 400)
7
8
6
9
5
10
4
3
11
2
13
12
1
250°C
200
150
7°C/min
100
Cl(CH₂CH₂O)ₙCH₂CH₂Cl
(POEG 600)
9
10
8
11
12
7
13
6
17
16
15
14
5
4
3
2
1
350°C
300
250
200
150
7°C/min
105

Fig. 1.

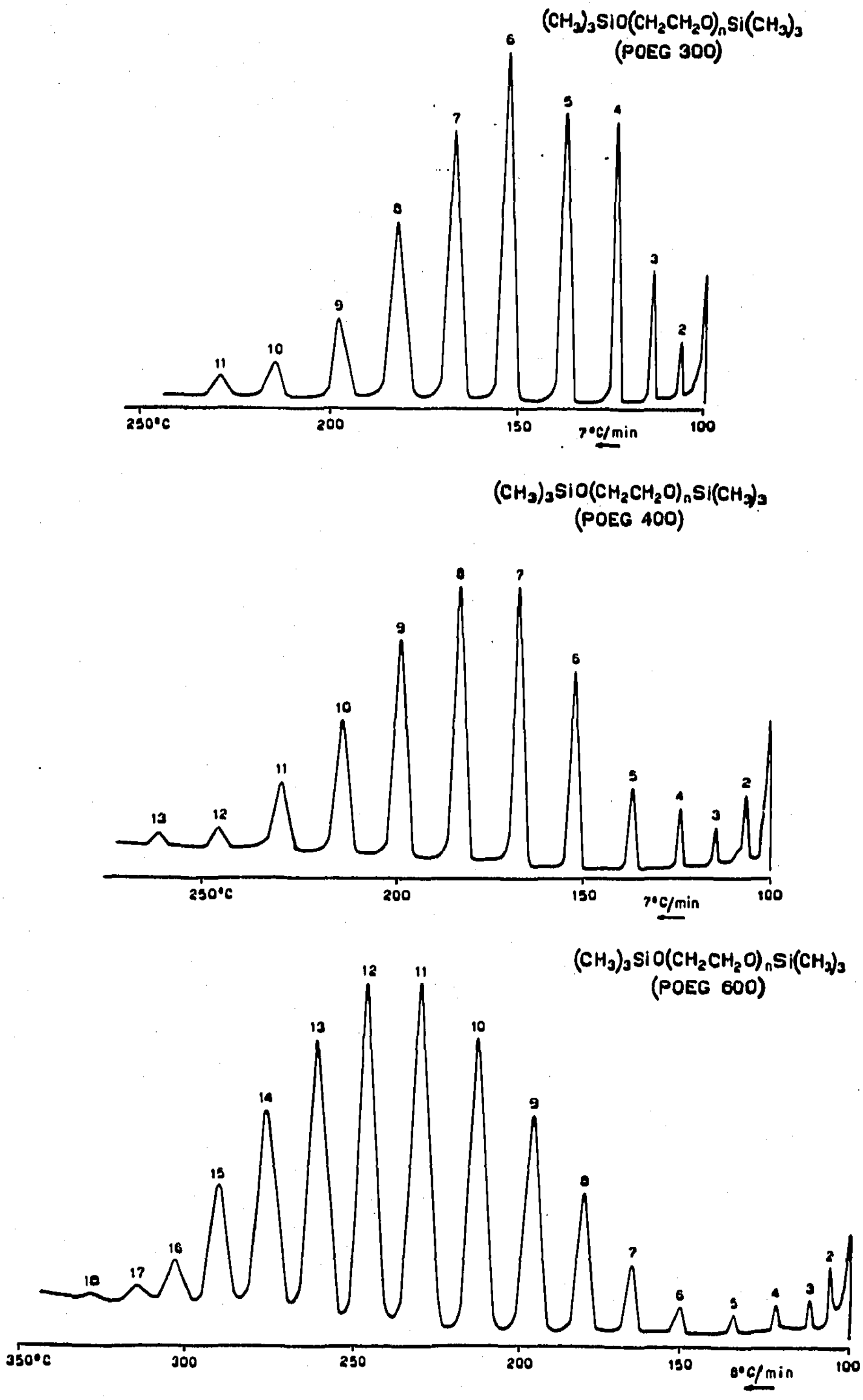
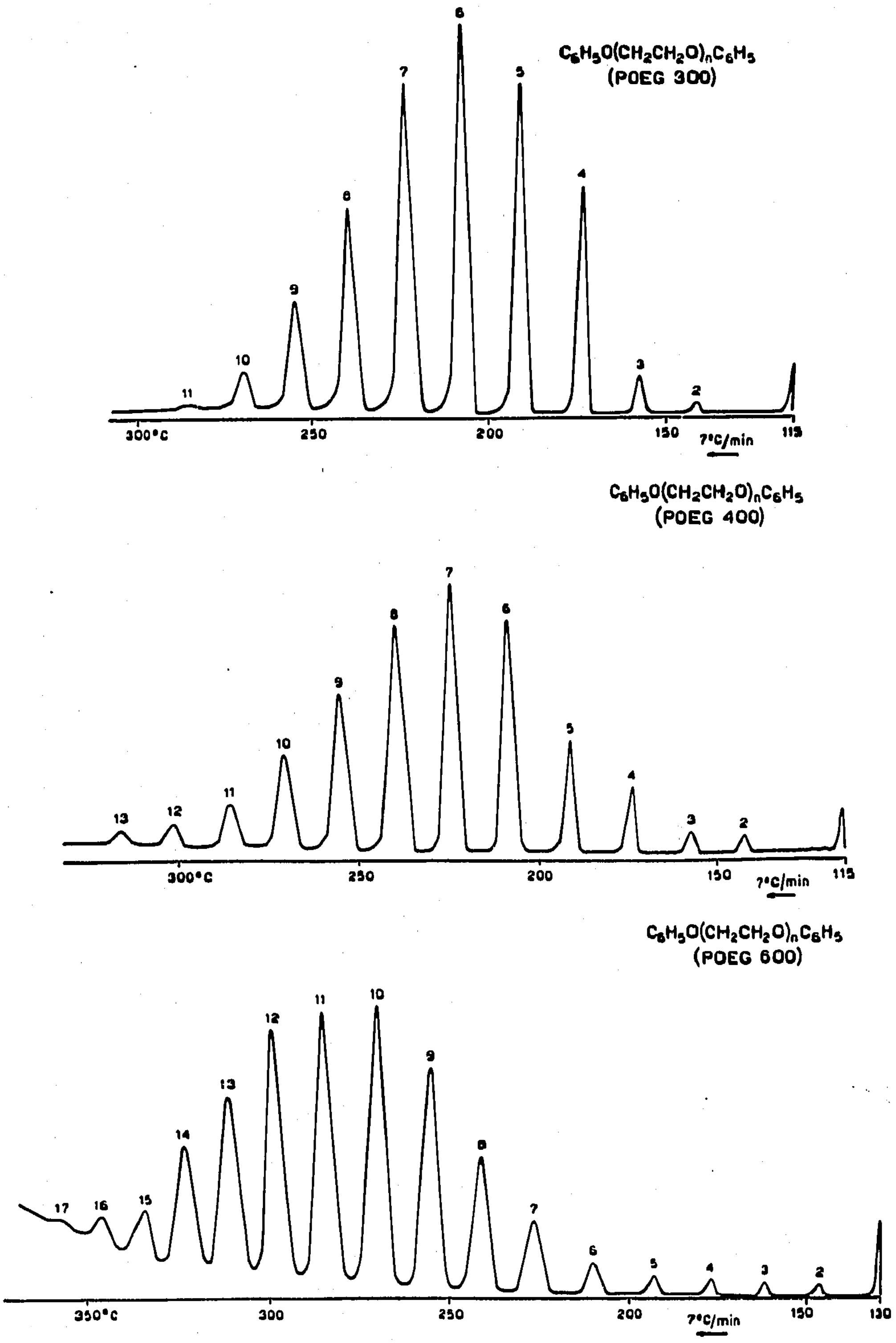


Fig. 1 *(continued)*.



$C_6H_5O(CH_2CH_2O)_nC_6H_5$
(POEG 300)

$C_6H_5O(CH_2CH_2O)_nC_6H_5$
(POEG 400)

$C_6H_5O(CH_2CH_2O)_nC_6H_5$
(POEG 600)

Fig. 1 *(continued)*.

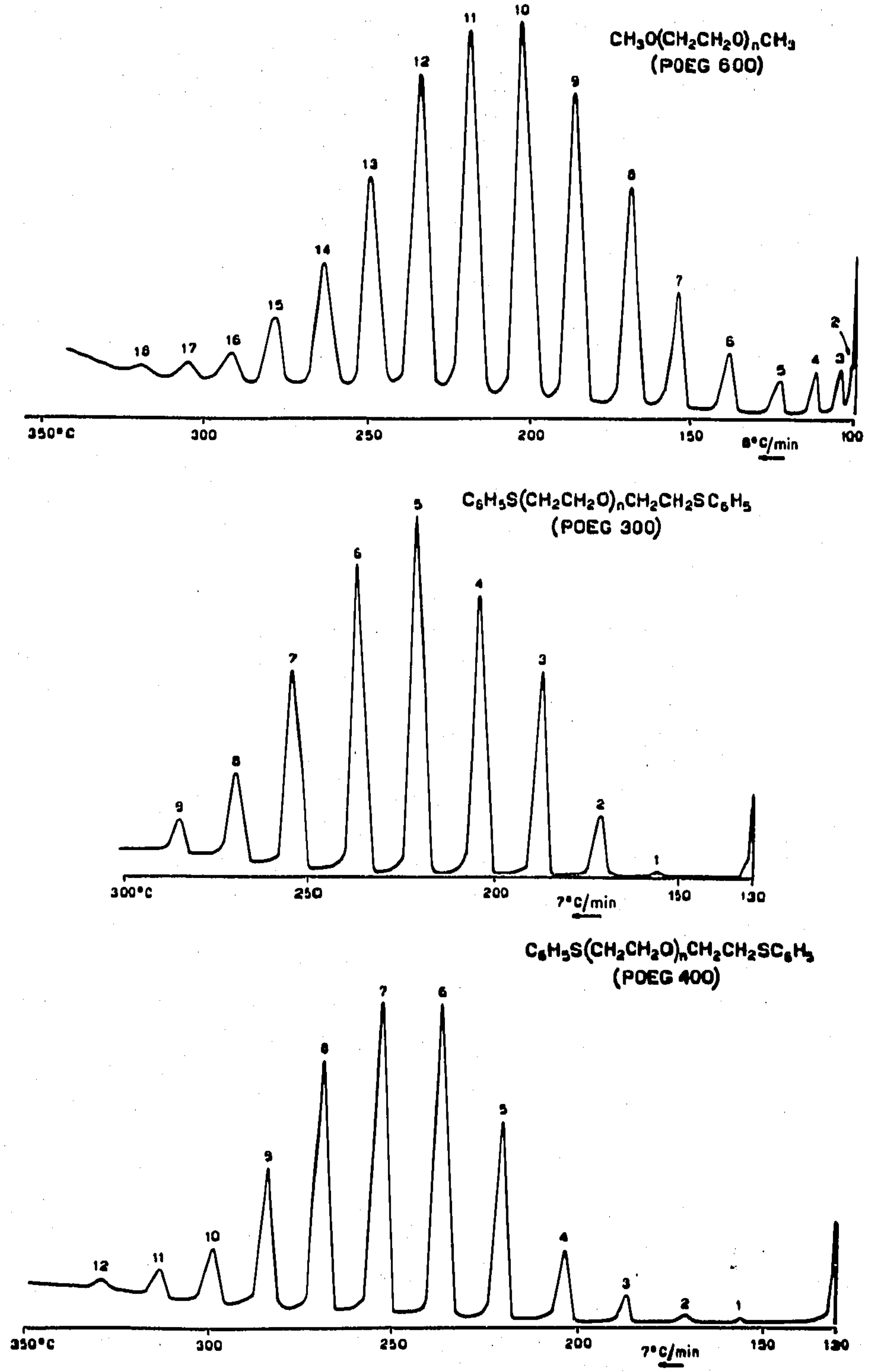


Fig. 1. Gas chromatograms of the various derivatives of polyethylene glycol products with a mean molecular weight of 300, 400, and 600 (PEG 300, PEG 400, and PEG 600). The number of peaks gives the value of *n*.

This paper deals with the gas chromatographic determination of the volatility and the thermal stability of polyethylene glycol and its dimethyl, diphenyl, and bis-trimethylsilyl ethers as well as $Cl(CH_2CH_2O)_nCH_2CH_2Cl$ (the replacement of the OH group by chlorine raises the volatility) and $PhS(CH_2CH_2O)_nCH_2CH_2S$ Ph (to find out what effect the introduction of sulphur has on the chromatographic behaviour).

## EXPERIMENTAL

The work was done with a Wilkens Aerograph 1521-1 fitted with a flame-ionization detector and a linear temperature programmer. We used a stainless steel column (22 cm in length and $\frac{1}{8}$ in. internal diameter), packed with 60–80 mesh silanized Chromosorb W impregnated with 5% of silicone-gum rubber SE-30. The injection point temperature varied with the compounds between 375 and 400°, the detector temperature being 375°. The temperature was raised from 100 to 350° at a rate of 7 or 8°/min. The flow rate of the carrier nitrogen was 54 ml/min.

To minimize the retention time of the higher molecular-weight products, we chose the shortest column that still separated the fractions. Under the analytical conditions used, the column selected could resolve alkanes differing by one methylene group. Furthermore, we chose a low-activity support and a low-volatility stationary phase. The amount of the latter should not be less than 5%, since otherwise the support adsorbs, particularly in the case of higher molecular-weight samples. It was found essential to stabilize the column at 300° for at least 24 h before use, possibly by using the temperature programmer several times. The chosen flow rate of nitrogen gave the best results. With this column, the effective peak number[12] for the $n$-$C_{22}$/$n$-$C_{23}$ paraffins was 0.3.

The three polyethylene glycol samples were industrial products (ex Chemische Werke Hüls) with stated mean molecular weights of 300, 400, and 600. Hexaethylene glycol, prepared by the method of FORDYCE, *et al.*[9], was converted into the appropriate derivatives which were used as internal standards. Thionyl chloride was used to prepare the dichloro derivatives[9], and these were then converted into the dimethyl, the diphenyl, and the bis-thiophenoxy derivatives by condensation with sodium methoxide, phenoxide, and thiophenoxide by the general method of CRETCHER AND PITTENGER[10]. The TMS derivatives were prepared with the aid of hexamethyldisilazane and trimethylchlorosilane[11]. The reagent was always in excess to maximize the conversion of the polyethylene glycol. Moisture was removed from the reagents and the equipment, the polyethylene glycol being dried for 6 h at 80° at a reduced pressure of 1 mm Hg. The preparations are briefly described below.

To prepare the dichloro derivatives, a solution of 0.01 mole of polyethylene glycol in 5 ml of pyridine was treated in a 50 ml flask with 0.03 mole (50% excess) of thionyl chloride, added dropwise and with vigorous agitation. The reaction mixture was kept for $\frac{1}{2}$ h at 80°, and then cooled. The residue was extracted with three 10-ml portions of diethyl ether, and the ether extracts were combined, treated with 0.5 g of sodium carbonate, and filtered. The filter was washed with 10 ml of diethyl ether, and the filtrate was freed from the solvent and impurities by heating at 80° and 10 mm Hg.

To prepare the bis-trimethylsilyl derivatives, 0.1 ml of hexamethyldisilazane and 0.05 ml of trimethylchlorosilane were introduced into a small test-tube containing

5 mg of polyethylene glycol in 0.2 ml of pyridine. The reactants were mixed and allowed to stand for 5 min.

The dimethyl derivatives were prepared by the dropwise addition of 0.005 mole of the dichloro derivative to 0.015 mole (50% excess) of sodium methoxide (prepared by mixing 0.35 g of metallic sodium with 15 ml of methanol). The solution was agitated for 10 min, the solvent distilled off, and the residue heated for 2 h at 70°. Cooling was followed by extraction with two 10-ml portions of diethyl ether, filtration, and the removal of the solvent by heating for 2 h at 40° and 0.5 mm Hg.

The diphenyl derivatives were prepared by mixing 0.02 mole of phenol with 0.015 mole of a methanolic solution of sodium methoxide (prepared as described above). The methanol was taken off under vacuum, and 0.005 moles of the dichloro derivative were added dropwise. The mixture was heated for 2 h at 120°, cooled, and extracted with five 5-ml portions of diethylether. The extracts were combined and freed from the solvent and phenol at 60° and 0.1 mm Hg.

To prepare the bis-thiophenoxy derivatives, 0.02 moles of thiophenol were introduced into 0.015 mole of a methanolic solution of sodium methoxide (prepared as described above). The methanol was distilled off, 0.005 moles of the dichloro derivative were added, and the reaction mixture was heated at 80° for 4 h. The excess thiophenol was then distilled off at 100–120° and 0.5 mm Hg.

## RESULTS

The chromatograms in Fig. 1 show the molecular-weight fractionation of the various derivatives of polyethylene glycol (PEG) samples with a mean molecular weight of 300, 400, and 600. Table 1 contains the values for the elution temperature

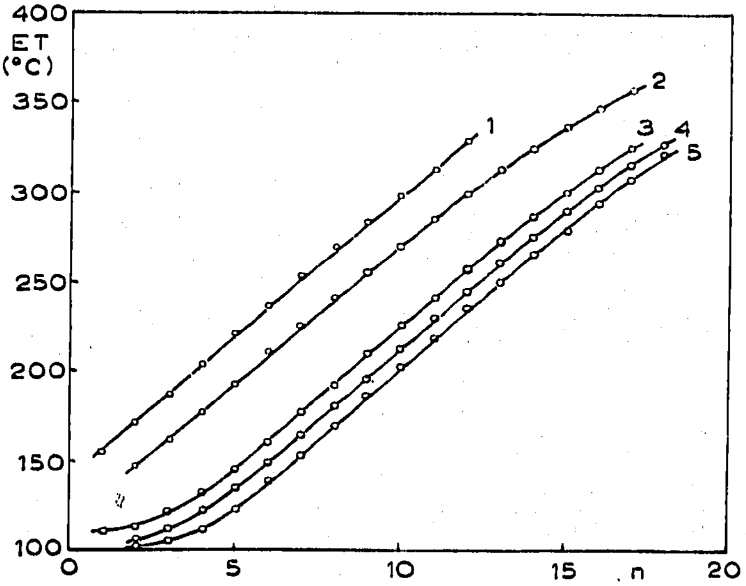


Fig. 2. Variation of the elution temperature ET with the degree of polymerization $n$ for the bis-thiophenoxy (1), diphenyl (2), dichloro (3), bis-trimethylsilyl (4), and the dimethyl (5) derivatives of polyethylene glycol.

TABLE I

GAS CHROMATOGRAPHIC RESULTS OF THE MOLECULAR-WEIGHT FRACTIONATION OF POLYETHYLENE GLYCOL DERIVATIVES

$n$ = degree of polymerization; ET = elution temperature (°C); A = peak area (%); $x_n$ = mole fraction (%); tr = traces.

| $n$ | $Cl(CH_2CH_2O)_nCH_2CH_2Cl$ | | | | | | | | | $(CH_3)_3SiO(CH_2CH_2O)_nSi(CH_3)_3$ | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PEG 300 | | | PEG 400 | | | PEG 600 | | | PEG 300 | | | PEG 400 | | | PEG 600 | | |
| | ET | A, % | $x_n$, % | ET | A, % | $x_n$, % | ET | A, % | $x_n$, % | ET | A, % | $x_n$, % | ET | A, % | $x_n$, % | ET | A, % | $x_n$, % |
| 1 | 106 | tr | — | 106 | tr | — | 111 | tr | — | — | — | — | — | — | — | — | — | — |
| 2 | 111 | 0.94 | 1.74 | 111 | 0.80 | 1.72 | 114 | 0.44 | 1.16 | 106 | 0.80 | 1.37 | 106 | 0.70 | 1.40 | 106 | 0.33 | 0.86 |
| 3 | 119 | 6.22 | 9.34 | 119 | 2.13 | 3.71 | 122 | 0.82 | 1.76 | 114 | 3.01 | 4.40 | 114 | 0.89 | 1.52 | 113 | 0.31 | 0.68 |
| 4 | 131 | 12.09 | 15.26 | 132 | 4.34 | 6.35 | 132 | 0.99 | 1.78 | 124 | 10.36 | 13.17 | 123 | 1.86 | 2.76 | 123 | 0.33 | 0.63 |
| 5 | 144 | 21.28 | 23.15 | 145 | 9.79 | 12.34 | 146 | 1.90 | 2.94 | 137 | 16.38 | 18.42 | 136 | 4.01 | 5.28 | 135 | 0.29 | 0.50 |
| 6 | 161 | 22.81 | 21.81 | 161 | 16.29 | 18.05 | 161 | 3.72 | 5.07 | 153 | 22.75 | 22.93 | 152 | 10.60 | 12.50 | 150 | 0.60 | 0.92 |
| 7 | 177 | 17.03 | 14.52 | 177 | 19.86 | 19.62 | 177 | 8.16 | 9.91 | 167 | 21.14 | 19.33 | 167 | 18.90 | 20.21 | 165 | 1.92 | 2.65 |
| 8 | 193 | 10.67 | 8.21 | 193 | 19.18 | 17.10 | 193 | 14.62 | 16.02 | 182 | 15.02 | 12.56 | 182 | 22.15 | 21.65 | 181 | 4.72 | 5.96 |
| 9 | 209 | 5.10 | 3.57 | 210 | 14.45 | 11.74 | 210 | 19.25 | 19.22 | 197 | 6.08 | 4.68 | 198 | 19.00 | 17.11 | 196 | 9.04 | 10.52 |
| 10 | 226 | 2.21 | 1.42 | 226 | 7.68 | 5.73 | 226 | 19.19 | 17.60 | 213 | 2.57 | 1.88 | 213 | 12.49 | 10.43 | 213 | 14.18 | 15.29 |
| 11 | 243 | 1.65 | 0.98 | 242 | 3.38 | 2.33 | 241 | 13.81 | 11.71 | 228 | 1.89 | 1.26 | 229 | 6.62 | 5.15 | 230 | 17.58 | 17.65 |
| 12 | — | — | — | 259 | 1.16 | 0.75 | 257 | 9.17 | 7.23 | — | — | — | 245 | 1.78 | 1.30 | 245 | 17.02 | 16.01 |
| 13 | — | — | — | 273 | 0.94 | 0.56 | 272 | 4.39 | 3.24 | — | — | — | 262 | 1.00 | 0.69 | 261 | 14.18 | 12.54 |
| 14 | — | — | — | — | — | — | 286 | 2.12 | 1.46 | — | — | — | — | — | — | 275 | 10.53 | 8.84 |
| 15 | — | — | — | — | — | — | 299 | 0.92 | 0.60 | — | — | — | — | — | — | 290 | 6.16 | 4.87 |
| 16 | — | — | — | — | — | — | 312 | 0.50 | 0.30 | — | — | — | — | — | — | 303 | 2.06 | 1.55 |
| 17 | — | — | — | — | — | — | 324 | tr | — | — | — | — | — | — | — | 315 | 0.75 | 0.53 |
| 18 | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — | 327 | tr | — |

TABLE I (*continued*)

| *n* | $CH_3O(CH_2CH_2O)_nCH_3$ | | | $C_6H_5O(CH_2CH_2O)_nC_6H_5$ | | | | | | | | | $C_6H_5S(CH_2CH_2O)_nCH_2CH_2SC_6H_5$ | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *PEG 600* | | | *PEG 300* | | | *PEG 400* | | | *PEG 600* | | | *PEG 300* | | | *PEG 400* | | |
| | *ET* | *A*, % | $x_n$, % | *ET* | *A*, % | $x_n$, % | *ET* | *A*, % | $x_n$, % | *ET* | *A*, % | $x_n$, % | *ET* | *A*, % | $x_n$, % | *ET* | *A*, % | $x_n$, % |
| 1 | — | — | — | — | — | — | — | — | — | — | — | — | 156 | tr | — | 156 | tr | — |
| 2 | 102 | tr | — | 141 | 0.29 | 0.49 | 143 | 0.69 | 1.30 | 147 | 0.39 | 0.93 | 173 | 3.06 | 4.26 | 172 | 0.43 | 0.69 |
| 3 | 105 | 0.51 | 1.40 | 158 | 2.94 | 4.26 | 158 | 1.24 | 2.00 | 162 | 0.51 | 1.05 | 188 | 11.78 | 14.50 | 187 | 1.37 | 1.96 |
| 4 | 112 | 0.81 | 1.78 | 174 | 10.36 | 13.09 | 174 | 3.16 | 4.44 | 177 | 0.66 | 1.18 | 205 | 18.45 | 20.34 | 204 | 4.21 | 5.38 |
| 5 | 124 | 0.78 | 1.43 | 191 | 17.63 | 19.77 | 191 | 6.86 | 8.56 | 193 | 0.82 | 1.30 | 221 | 24.61 | 24.57 | 221 | 12.80 | 14.81 |
| 6 | 139 | 1.79 | 2.83 | 208 | 22.63 | 22.80 | 208 | 16.46 | 18.46 | 211 | 1.63 | 2.33 | 237 | 21.45 | 19.57 | 237 | 23.32 | 24.66 |
| 7 | 154 | 4.08 | 5.64 | 224 | 22.20 | 20.31 | 224 | 21.53 | 21.93 | 226 | 4.31 | 5.59 | 253 | 13.12 | 11.02 | 253 | 23.63 | 23.10 |
| 8 | 170 | 8.90 | 10.94 | 240 | 14.26 | 11.95 | 239 | 21.54 | 20.08 | 241 | 7.84 | 9.30 | 269 | 5.51 | 4.28 | 269 | 18.16 | 16.38 |
| 9 | 187 | 13.77 | 15.23 | 255 | 7.22 | 5.56 | 255 | 15.17 | 13.04 | 255 | 13.03 | 14.26 | 284 | 2.02 | 1.46 | 283 | 9.81 | 8.24 |
| 10 | 203 | 17.59 | 17.70 | 270 | 2.47 | 1.77 | 270 | 7.77 | 6.20 | 270 | 16.91 | 17.16 | — | — | — | 298 | 3.78 | 2.97 |
| 11 | 219 | 16.73 | 15.44 | 284 | tr | — | 285 | 3.20 | 2.38 | 285 | 16.55 | 15.68 | — | — | — | 312 | 1.88 | 1.39 |
| 12 | 235 | 14.42 | 12.29 | — | — | — | 300 | 1.43 | 0.99 | 299 | 15.20 | 13.49 | — | — | — | 328 | 0.60 | 0.42 |
| 13 | 250 | 9.56 | 7.57 | — | — | — | 316 | 0.95 | 0.62 | 313 | 10.88 | 9.08 | — | — | — | — | — | — |
| 14 | 265 | 5.49 | 4.05 | — | — | — | — | — | — | 324 | 7.14 | 5.63 | — | — | — | — | — | — |
| 15 | 279 | 3.07 | 2.13 | — | — | — | — | — | — | 336 | 2.65 | 1.98 | — | — | — | — | — | — |
| 16 | 294 | 1.28 | 0.83 | — | — | — | — | — | — | 347 | 1.22 | 0.86 | — | — | — | — | — | — |
| 17 | 307 | 0.89 | 0.55 | — | — | — | — | — | — | 357 | 0.26 | 0.18 | — | — | — | — | — | — |
| 18 | 321 | 0.33 | 0.19 | — | — | — | — | — | — | — | — | — | — | — | — | — | — | — |

(ET), the relative peak area (A), and the molar fraction ($x_n$) of the constituents. Hexaethylene glycol derivatives were used as internal standards.

Maximum volatility and thermal stability and minimum energy of adsorption on the support are the characteristics of the most suitable type of derivative for the determination of $n$ by GLC. The volatility of derivatives with the same value of $n$ decreases as follows: dimethyl $>$ bis-trimethylsilyl $>$ dichloro $>$ diphenyl $>$ bis-thiophenoxy derivatives. The elution temperature within a series varies linearly with $n$ over a wide range (see Fig. 2). The deviations from linearity at high $n$ values are probably due to difficulties in keeping the temperature-programming linear and the flow rate of the carrier gas constant at high temperatures. In the linear domain between about 150 and 300°, the graphs for all the derivatives have the same slope of about 15°/$n$. In addition, using the more volatile derivatives (dimethyl and bis-trimethylsilyl derivatives), one can separate compounds with an $n$ of up to 18, *i.e.* up to a molecular weight of about 900.

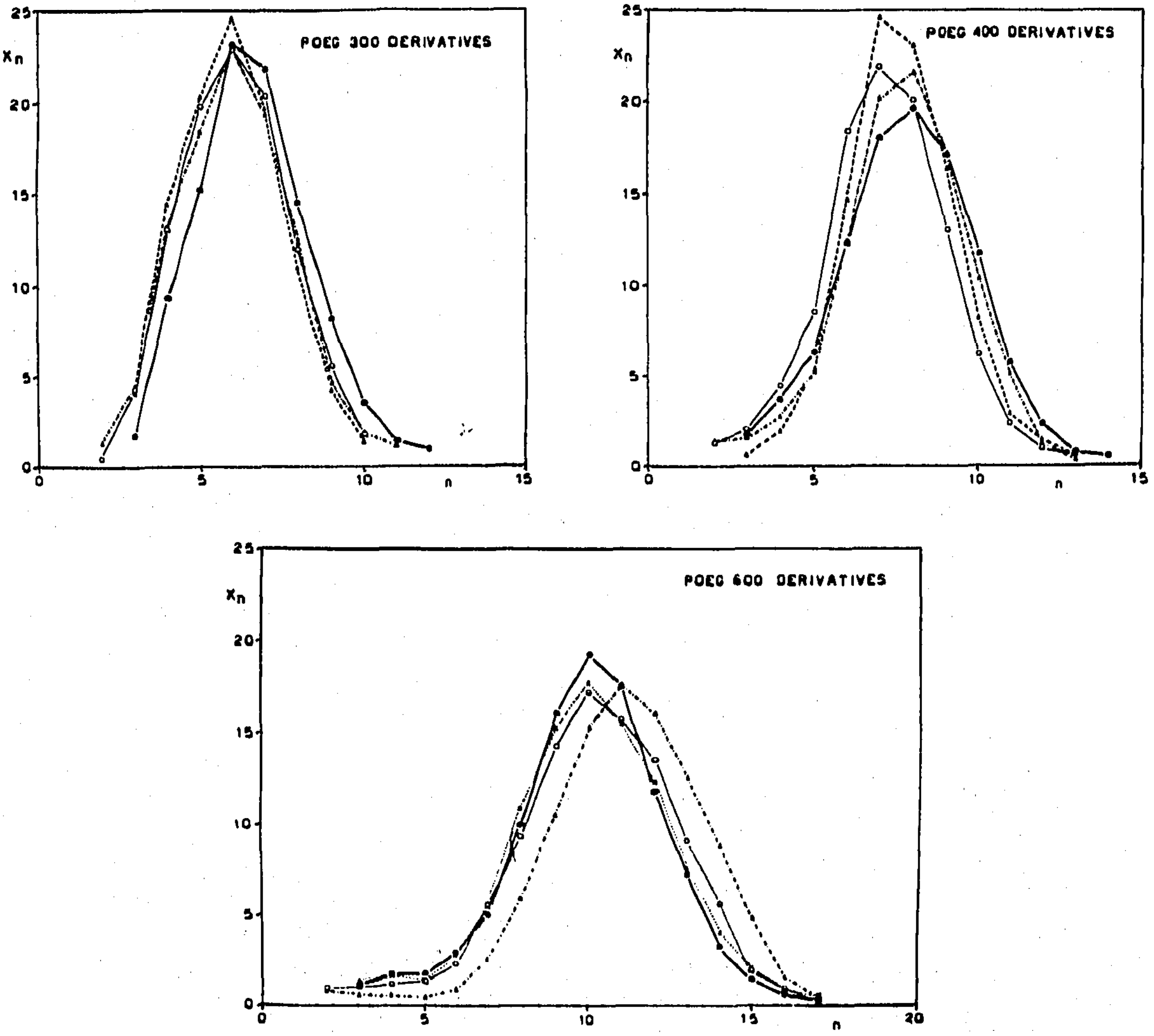


Fig. 3. Distribution of the degree of polymerization $n$ for the dichloro (●), bis-trimethylsilyl (▲), dimethyl (×), diphenyl (○), and the bis-thiophenoxy (△) derivatives of polyethylene glycol 300, 400, and 600 (in the case of the dichloro and the bis-thiophenoxy derivatives, $n$ refers to the starting polyethylene glycol product).

The replacement of oxygen by sulphur in the molecule lowers the volatility, even if the fact that it also reduces the value of $n$ by one is taken into account. However, even conversion into the bis-thiophenoxy derivatives facilitates the resolution of compounds with a molecular weight exceeding 750.

The derivatives generally have a fairly good thermal stability, permitting an evaporator temperature of 375° in all cases. With the bis-trimethylsilyl, the dimethyl, and the diphenyl derivatives, this temperature can be raised to 400° without any pyrolysis occurring.

Adsorption on the support, which is particularly a hazard with compounds having a higher $n$ value and less volatile substituents, was found the smallest in the case of the bis-trimethylsilyl and the dimethyl derivatives.

The most suitable type of derivative can be chosen on the basis of the distribution curves in Fig. 3, though it must be ascertained in each particular case that polyethylene glycol is quantitatively converted into the derivative. The curves for the derivatives of PEG 300 are superimposable, and so are those for the derivatives of PEG 400. In the case of the derivatives of PEG 600, on the other hand, the distribution curve for the bis-trimethylsilyl derivatives is displaced towards higher $n$ values, probably because of the higher volatility and because of the fact that these derivatives were prepared in a single step. Although the dimethyl derivatives are more volatile, they were prepared *via* the dichloro derivatives, and the possibility of a systematic shift in the distribution during this reaction cannot be excluded. The good agreement between the curves for the dimethyl derivatives and those for the dichloro derivatives indicates that the conversion into the dimethyl compounds is almost quantitative, which agrees with the high yields; the chlorination of polyethylene glycol must therefore be less complete.

These results show that, under the present experimental conditions, the bis-trimethylsilyl derivatives are the most suitable for the gas chromatographic analysis of polyethylene glycol products, since they have a high volatility, high thermal stability, low energy of adsorption on the support, and a simpler synthesis which probably ensures a more complete conversion.

## ACKNOWLEDGEMENT

The authors wish to thank Chemische Werke Hüls (Marl/Kreis Recklinghausen, Germany) for supplying the polyethylene glycol samples.

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