Journal of Chromatography, 109 (1975) 101–106

CHROM. 8211

SEPARATION OF ALKALI METAL CARBOXYBENZENESULPHONATES AND THEIR 2-HYDROXYETHYL ESTERS ON SEPHADEX LH-20 GEL

J. VEJROSTA and J. MÁLEK*

Institute of Chemical Process Fundamentals, Czechoslovak Academy of Sciences, 165 02 Prague-Suchdol (Czechoslovakia)

(Received January 30th, 1975)

SUMMARY

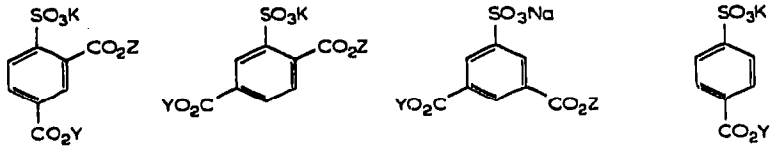
Mixtures of alkali metal carboxybenzenesulphonates and their 2-hydroxyethyl and bis(2-hydroxyethyl) esters, obtained by esterification of the carboxybenzenesulphonates with ethylene glycol at elevated temperatures, were readily separated by chromatography on Sephadex LH-20 gel at pH 8.5 by using potassium dihydrogen orthophosphate–disodium hydrogen orthophosphate buffer as eluent.

INTRODUCTION

Potassium 2,4-dicarboxybenzenesulphonate (I), potassium 2,5-dicarboxybenzenesulphonate (II) and sodium 3,5-dicarboxybenzenesulphonate (III) react with ethylene glycol at elevated temperatures to form the corresponding bis(2-hydroxyethyl) esters (V–VII)[1,2], which are important co-monomers in the preparation of linear polyesters; similarly, potassium 4-carboxybenzenesulphonate (IV) gives potassium 4-(2-hydroxyethoxycarbonyl)benzenesulphonate (VIII)[2]. The starting material III is converted into the bis(2-hydroxyethyl) ester VII via an intermediate, assumed to be the 2-hydroxyethyl ester XIII, thus yielding a three-component mixture in the initial stage of the reaction; the course of the esterification of I and II is even more complicated owing to the occurrence of two intermediate compounds, probably the isomeric 2-hydroxyethyl esters IX–X and XI–XII, respectively.

The determination of time–concentration changes in the mixtures obtained by the reaction of I–III with the diol, which was necessary for our kinetic study of the above esterification reactions, was not possible by using classical analytical methods. The successive separation of the reaction components and their polarography, applied with success to the analysis of the complex reaction mixture resulting from the esterification of terephthalic acid with ethylene glycol[3], could not be employed in this instance because of the comparatively high solubility in water of the carboxybenzenesulphonates I–IV and esters V–VIII, their extremely low solubility in organic

* Author to whom enquiries should be addressed.



		Y = Z = H:	
I	II	III	IV
		Y = Z = CH_2CH_2OH:	
V	VI	VII	VIII
		Y = CH_2CH_2OH, Z = H:	—
IX	XI	XIII	
		Y = H, Z = CH_2CH_2OH:	—
X	XII	—	

solvents and their chemical similarity. The successful separation of aliphatic and aromatic carboxylic acids has been achieved previously by gel chromatography on Sephadex G-25 (ref. 4), G-10 (refs. 5–8), LH-20 (ref. 8) and 832 (ref. 9) gels and by ion-exchange chromatography on Zipax SAX columns[10]. Gel chromatography on Sephadex G-25 (ref. 11) and the ion-exchange separation and determination of aromatic sulphonic acids on Amberlite XAD-2 resin[12], Bio-Rex 5 resin[13] and Zipax SAX columns[14] have also been reported. It was therefore hoped that the separation and quantitative determination of compounds I–XIII, bearing carboxylic or ester as well as sulphonic acid groups, might be carried out by using gel chromatography on suitable gel packings. This assumption was supported by a recent finding that the disproportionation of III which takes place on Sephadex gels in purely aqueous solutions could be completely suppressed by using buffers as eluents[15].

EXPERIMENTAL

Chemicals

Potassium and sodium carboxybenzenesulphonates (I–IV) were analytical-reagent grade products (Research Institute for Organic Syntheses, Czechoslovakia) of 99.3–99.9% purity. Bis(2-hydroxyethyl) esters (V–VII) and the 2-hydroxyethyl ester (VIII) were prepared by esterification of I–III and IV, respectively, with ethylene glycol as described previously[16]; their purities, verified by determination of the saponification numbers and alkali metal contents, were higher than 98.5%. *p*-Toluenesulphonic acid (Lachema, Brno, Czechoslovakia), used as a model compound, was of analytical-reagent grade. Aqueous solutions of these compounds saturated at 15° were used for chromatography. The esterification mixtures were prepared[16] by reacting I, II, III or IV with ethylene glycol (chromatographically pure) (initial molar ratio 1:20) in the presence of tin (II) oxalate as catalyst (0.35% on the acid used) and triethylamine (5% on the acid; used to inhibit diethylene glycol formation) under nitrogen at 197°; samples (1.0 ml) for chromatography were withdrawn from the reaction mixture with a heated pipette, placed into pre-cooled ampoules and chromatographed without further dilution. Sephadex LH-20 gel and Blue Dextran 2000

(internal standard) were obtained from Pharmacia, Uppsala, Sweden. Britton–Robinson buffer of ionic strength $I = 0.025$ (pH range 2.16–8.40) and potassium dihydrogen orthophosphate–disodium hydrogen orthophosphate buffer (pH 8.5) were used as eluents.

Gel chromatography

The dependence of the distribution coefficients (K_D) on pH values for the carboxybenzenesulphonates (I–IV) and *p*-toluenesulphonic acid was measured on a glass column, 0.36 cm in diameter, packed[17] with Sephadex LH-20 gel to a height of 68 cm. Degassed Britton–Robinson buffer was passed up the column with a pulsing positive displacement MC 300 pump (Mikrotechna, Prague, Czechoslovakia) with a damping system to reduce pressure fluctuations; the pressure at the column inlet was measured with a Bourdon manometer. Solute samples (10–30 μl) were introduced on to the column with a Hamilton syringe. The effluent from the column was monitored continuously with a differential UV analyzer measuring the absorbance at 254 nm (Development Works, Czechoslovak Academy of Sciences, Prague, Czechoslovakia) and connected to a TZ21S linear recorder (Laboratory Instruments, Prague, Czechoslovakia). The elution volumes measured by means of a syphon integral flow meter and expressed in millilitres were reproducible to within $\pm$ 2%. Esterification mixtures were fractionated in a similar manner on a stainless-steel column, 0.8 cm in diameter, and packed with Sephadex LH-20 up to a height of 120 cm; the eluent was potassium dihydrogen orthophosphate–disodium hydrogen orthophosphate buffer (pH 8.5). The same system was used for determining the elution volumes of the pure carboxybenzenesulphonates (I–IV), the bis(2-hydroxyethyl) esters (V–VII) and of the 2-hydroxyethyl ester (VIII). All fractionation experiments on the stainless-steel column were carried out at room temperature at a flow-rate of 0.90 ml/min. The K_D values were calculated from the equation $K_D = (V_e - V_0)/V_i$, where V_e is the elution volume of the solute, V_0 the void volume of the column and V_i the internal aqueous volume of the gel beads. V_e was obtained from the recorder chart; V_0 determined as the elution volume of Blue Dextran 2000, was 1.91 ml; V_i, calculated as the product of the water regain (manufacturer's value) and the dry weight of the gel, was 2.90 ml.

RESULTS AND DISCUSSION

The dependence of K_D on pH for the alkali metal carboxybenzenesulphonates (I–IV) and *p*-toluenesulphonic acid is shown in Fig. 1. The approximate pK_a value for IV, which was derived from this dependence according to Brook and Housley[6], is 3.7; which is very close to that reported[18] for *p*-carboxybenzenesulphonic acid (3.72). Complete curves for other carboxybenzenesulphonates in this series, whose dissociation constants are not available, could not be determined owing to the instability of Sephadex gel in solutions of pH < 2. The K_D *versus* pH plot indicates that compounds I–IV are adsorbed by the gel at pH < 4 and that their mixtures could be separated in this pH region.

Preliminary experiments have shown that potassium dihydrogen orthophosphate–disodium hydrogen orthophosphate buffer solution (I 0.025, pH 8.5) is a suitable system for the separation of alkali metal carboxybenzenesulphonates and

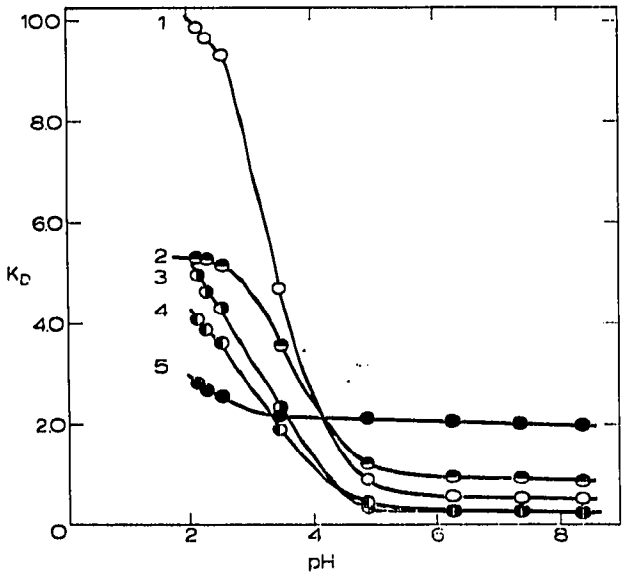


Fig. 1. Effect of pH on distribution coefficients (K_D) of sodium 3,5-dicarboxybenzenesulphonate (1), potassium 4-carboxybenzenesulphonate (2), potassium 2,5-dicarboxybenzenesulphonate (3), potassium 2,4-dicarboxybenzenesulphonate (4) and *p*-toluenesulphonic acid (5).

their 2-hydroxyethyl esters on Sephadex LH-20 gel. All esters were sufficiently stable under these conditions. Symmetrical peaks were obtained in all separation experiments. The results obtained for the gel chromatography of mixtures resulting from the esterification of IV with ethylene glycol (90-min reaction time) to give its 2-hydroxyethyl ester, VIII (Fig. 2), and from the esterification of III with the above diol (70-min reaction time) to give the corresponding bis(2-hydroxyethyl) ester, VII (Fig. 3), demonstrate the ability of this technique to resolve structurally related compounds of this series. The presence of IV and VIII as well as III and VII in these mixtures has been proved by comparison of elution volumes, read from the maxima of the corresponding peaks in Figs. 2 and 3, respectively, with those of authentic

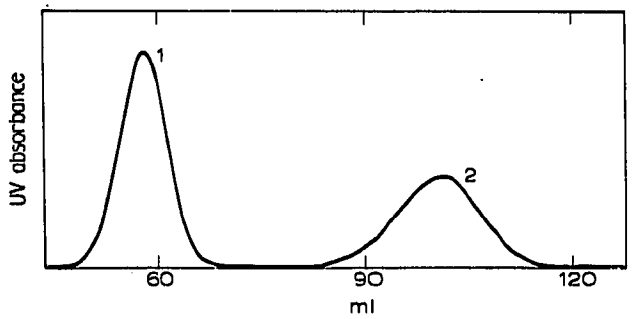


Fig. 2. Gel chromatogram of the separation of the reaction mixture from the esterification of potassium 4-carboxybenzenesulphonate (1) with ethylene glycol to give potassium 4-(2-hydroxyethoxycarbonyl)benzenesulphonate (2).

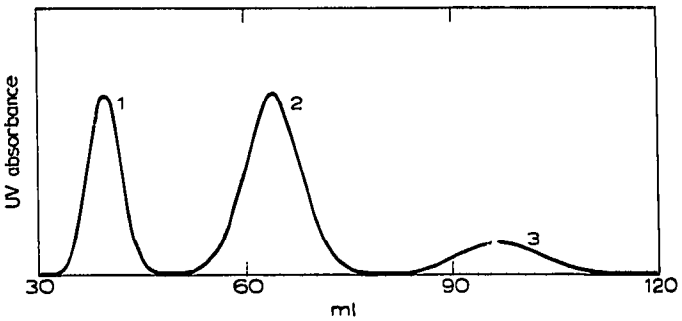


Fig. 3. Gel chromatogram of the separation of the reaction mixture from the esterification of sodium 3,5-dicarboxybenzenesulphonate (1) with ethylene glycol to give sodium 3-carboxy-5-(2-hydroxyethoxycarbonyl)benzenesulphonate (2) and sodium 3,5-bis(2-hydroxyethoxycarbonyl)benzenesulphonate (3).

compounds. The compound whose peak is located (Fig. 3) between that of the carboxybenzenesulphonate III and that of the bis-ester VII was assigned the structure of the yet unknown mono-ester XIII; the gradual disappearance of XIII from the mixture with increasing concentration of the bis-ester VII with time and the mass balance of the esterification mixture strongly support the assumed structure. A similar, although more complicated, situation was encountered in the gel chromatography of the mixture resulting from the esterification of the carboxybenzenesulphonate II with ethylene glycol to give the bis-ester VI (Fig. 4); the elution volumes of II and VI in the chromatogram were identical with those of pure authentic compounds. Fig. 4 shows the changes in concentrations of II and VI with time (35, 90 and 360 min) as well as those of two unknown compounds that are thought to be the isomeric mono-esters of II, *i.e.*, XI and XII. According to the electron-attracting ability of the sulphonic acid group and the expected steric hindrance influencing the reactivity of the *ortho*-carboxylic group of II, it is probable that the mono-ester present in higher

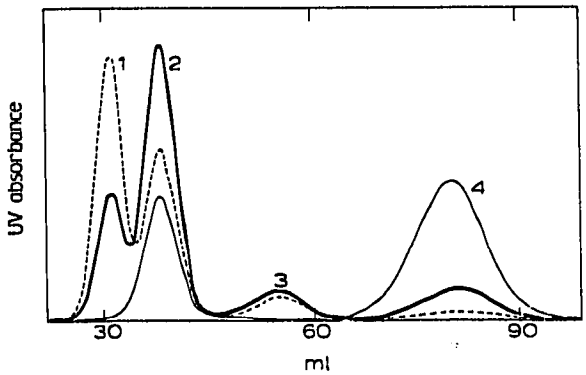


Fig. 4. Gel chromatogram of the separation of the reaction mixture from the esterification of potassium 2,5-dicarboxybenzenesulphonate (1) with ethylene glycol to give potassium 2-carboxy-5-(2-hydroxyethoxycarbonyl)benzenesulphonate (2), potassium 5-carboxy-2-(2-hydroxyethoxycarbonyl)-benzenesulphonate (3) and potassium 2,5-bis(2-hydroxyethoxycarbonyl)benzenesulphonate (4) after 35-min (broken line), 90-min (thick line) and 360-min (thin line) reaction times.

concentrations is potassium 2-carboxy-5-(2-hydroxyethoxycarbonyl)benzenesulphonate (XI). This assumption is in agreement with the relatively high concentration (Fig. 3) of the mono-ester formed transiently during the esterification of III. The gel chromatography of reaction mixtures produced by esterification of the carboxybenzenesulphonate I with ethylene glycol showed a chromatogram essentially identical with that given in Fig. 4. As confirmed by gel chromatography, unexpectedly no oligomers are formed in detectable amounts during the esterification of I–III under the conditions used. Elucidation of the structures of the mono-esters and the quantitative determination of all of the individual components in these esterification mixtures is the subject of a forthcoming study.

ACKNOWLEDGEMENT

The authors thank Mr. Z. Šír for measurements of pH values and for helpful discussions.

REFERENCES

1 J. Málek, J. Hradil and V. Bažant, *Ger. Pat.*, 1952735 (1970); *C.A.*, 73 (1970) 67054w.
2 J. Málek, M. Řeřichová and V. Lacko, *Czech. Pat. Appl.*, 8181 (1974).
3 M. Krumpolc and J. Málek, *Makromol. Chem.*, 171 (1973) 69.
4 R. Haavaldsen and T. Norseth, *Anal. Biochem.*, 15 (1966) 536.
5 A. J. W. Brook, *Chem. Ind. (London)*, (1968) 1434.
6 A. J. W. Brook and S. Housley, *J. Chromatogr.*, 42 (1969) 112.
7 A. J. W. Brook, *J. Chromatogr.*, 39 (1969) 328.
8 A. J. W. Brook and K. C. Munday, *J. Chromatogr.*, 47 (1970) 1.
9 J. Kučera, S. Pokorný and J. Čoupek, *J. Chromatogr.*, 88 (1974) 281.
10 J. Aurenge, *J. Chromatogr.*, 84 (1973) 285.
11 H. Steuerle, *Z. Anal. Chem.*, 220 (1966) 413.
12 M. W. Scoggins and J. W. Miller, *Anal. Chem.*, 40 (1968) 1155.
13 R. H. Stehl, *Anal. Chem.*, 42 (1970) 1802.
14 J. J. Kirkland, *Anal. Chem.*, 43 (1971) 37A.
15 M. Minárik and Z. Šír, *Collect. Czech. Chem. Commun.*, in press.
16 J. Málek and M. Řeřichová, *Chem. Prům.*, in press.
17 H. Determann, *Gel Chromatography*, Springer, Berlin, New York, 1968, p. 42.
18 A. Albert and E. P. Serjeant, *Ionization Constants of Acids and Bases*, Methuen, London, 1962, p. 134.