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GEL CHROMATOGRAPHY OF METALLOCENE DERIVATIVES ON CROSSLINKED POLYSTYRENE

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Summary

Beads of polystyrene crosslinked with 2% divinylbenzene swell in cyclohexane to provide a matrix which resolves effectively various derivatives of ferrocene in column chromatographic experiments. The separation effects seem to be achieved through weak interaction between solute and gel matrix rather than by molecular sieving, as is demonstrated by the different distribution coefficients for ferrocene, ruthenocene, and osmocene. The system also resolves other classes of substances, e.g. aromatic azo compounds.

Introduction

A survey of the literature in the field of preparative organometallic chemistry shows that the materials most commonly used for the chromatographic purification of new compounds are alumina, silica gel, and to some extent alkylated, crosslinked dextran (e.g. Sephadex LH-20). All these materials are subject to different kinds of limitations. The dextran contains residual hydroxy groups and is therefore unsuitable for the purification of a large number of organometallic substances. Alumina adsorbs strongly a host of compounds and may catalyze molecular rearrangements, e.g. racemization [1]. The materials mentioned above often demand the use of highly polar solvents.

The inorganic adsorbents are composed of particles differing in size and form which causes low flow rates in preparative columns. Recently, tightly crosslinked polystyrene beads in combination with tetrahydrofuran have been shown to be a useful matrix for the fractionation of different classes of organic compounds, the predominant separation mechanism being molecular sieving [2]. For some time, we have been engaged in the preparation of organometallic substrates and inhibitors of enzyme systems [3], and therefore needed efficient separation methods adaptable to a preparative scale. This communication describes the chromatographic separation of metallocenes and their derivatives on columns of polystyrene gel beads crosslinked with 2% divinylbenzene, using cyclohexane as solvent.

Materials and methods

Polystyrene beads crosslinked with different amounts of divinylbenzene were a gift of Dow Chemical Co., Midland, U.S.A. The experiments described below were conducted with X2 (2% divinylbenzene, 200-400 mesh) and X8 (8% divinylbenzene, 200-400 mesh). The solvents were of analytical grade and were obtained from Merck AG, Darmstadt, Germany. Ferrocene was obtained from Th. Schuchardt, München, and formyl ferrocene from EGA-Chemie, Heidenheim, Germany. The other organometallic compounds were synthesized according to or by modification of procedures found in the literature [4]. Another sample of hydroxymethyl ferrocene was obtained from Research Organic Inorganic Chemical Co., Sun Valley (U.S.A.).

The chromatographic columns consisted of Quickfit precision bore tubing closed at both ends with identical pistons fitted with TEFLON-sieves. The effluent was monitored continuously with a Uvicord II (LKB produkter, Stockholm) operating at 280 nm. To collect the effluents a fraction collector (Stålprodukter, Uppsala) was used. After evaporation of the solvent, the different fractions were characterized by their melting points, elementary analyses and NMR spectra.

The solvent regain of the polymers and the bed volume after swelling were determined by weighing a certain amount into a stoppered measuring cylinder. The volumes of the gel bed were noted before and after soaking in solvent over night, the weight of the swollen beads was obtained after transferring the gel slurry into a preweighed glassfilter and by centrifuging the solvent held between the beads [5].

Results and discussion

Table 1 shows that the beads used in our experiments are characterized by widely different solvent regains in different solvents and therefore also have different degrees of swelling. This applies to both X2 and X8 and characterizes these materials as true xerogels in contrast to macroreticular, rigid copolymer beads with rather fixed pore size (Ref. 5, p. 14). We tried to resolve different mixtures of metallocene derivatives on both X2 and X8 in various solvents. Poor resolution was obtained either in benzene, chloroform and tetrahydrofuran, or even in alcohols and alkanes, where the degree of swelling was low. The system

TABLE 1

SOLVENT REGAIN AND BED VOLUMES OF POLYSTYRENE GELS IN DIFFERENT SOLVENTS

Polymer	Solvent	Solvent regain (ml solvent/g dry gel)	Approx. bed volume (ml/g dry gel)
X2	Cyclohexane	0.96	2.7—2.9
	Benzene	2.79	5.3—5.5
	Chloroform	2.84	6.1—6.3
	Butanol-1	0.15	1.7—1.9
	Phenol	0.67	2.0—2.2
X8	Cyclohexane	0.03	1.6—1.8
	Tetrahydrofuran	0.92	2.5—2.8

TABLE 2

RETENTION OF METALLOCENE DERIVATIVES AND TWO AZO COMPOUNDS ON X2 IN CYCLOHEXANE[a]

Compound	Mol. weight	K_{av}
Ferrocene	186.0	1.1
Ruthenocene	231.7	1.3
Osmocene	320.2	1.5
α-Hydroxyethylferrocene	229.1	1.6
Hydroxymethylferrocene	216.0	2.3
Acetylferrocene	228.0	2.6
1,1′-Diacetylferrocene	270.1	3.9
trans-Azobenzene[b]	182.2	1.6
4-Dimethylaminoazobenzene[b]	225.3	2.6

[a] Column dimensions 35.6 × 1.2 cm; total volume 40.2 ml; void volume 16.1 ml; flow rate 15 ml/h. [b] The system also separates *trans*- and *cis*-azobenzene (unpublished experiments).

X2—cyclohexane worked exceptionally well and was studied in detail; it is now being used routinely for the separation of metallocene derivatives in our laboratory.

Table 2 summarizes part of the experiments carried out so far but includes

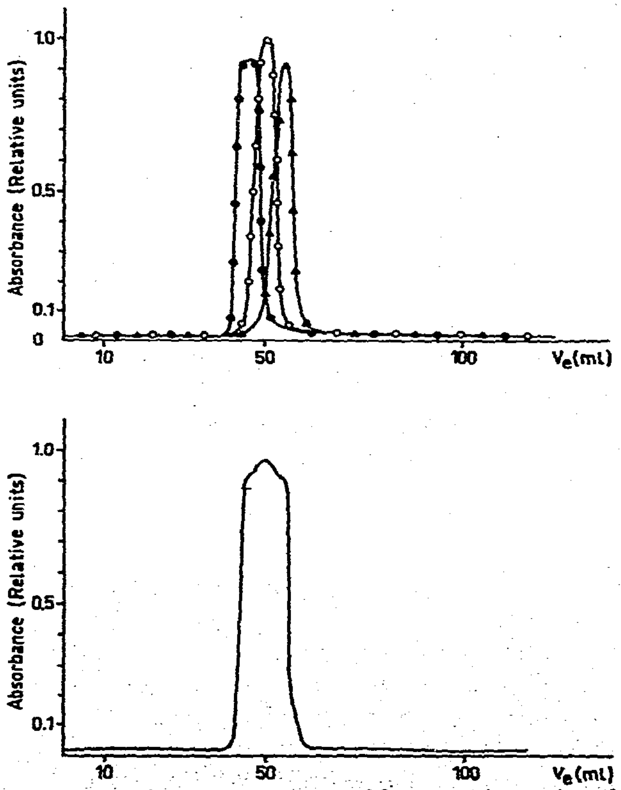

Fig. 1. Upper half: Separate runs of ferrocene (-●-●-●-), ruthenocene (-○-○-○-), and osmocene (-▲-▲-▲-) on X2—cyclohexane. Column dimensions and K_{av} values see Table 1. Lower half: Partial resolution of a mixture of the three metallocenes on the same column.

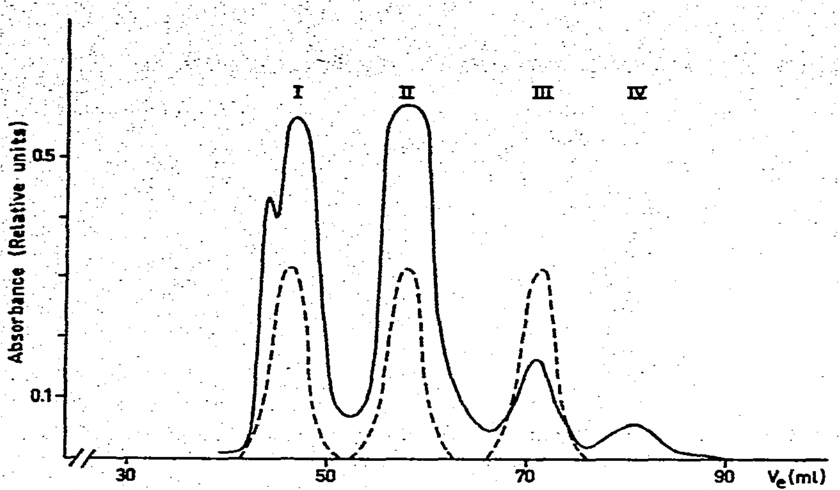

Fig. 2. Chromatographic purification of hydroxymethylferrocene on X2—cyclohexane. Solid line: Commercial sample of technical purity. Dotted line: Separate runs with reference samples, Peak I, ferrocene; peak II, α-hydroxyethylferrocene; Peak III, hydroxymethylferrocene. For column dimensions, see Table 1.

a few data on azo dyes. The retention of the solutes is expressed in terms of the distribution constant K_{av}, which equals $(V_e - V_0)/(V_t - V_0)$; V_e being the elution volume, V_0 the void volume, and V_t the total volume of the column [6]. It is obvious that the ferrocene is separated well from its mono- and di-acetyl derivatives, and hydroxymethylferrocene is separated well from the closely related α-hydroxyethylferrocene. Most notably, the migration rates differ between dicyclopentadienyl-iron, -ruthenium, and -osmium, so that a partial resolution could be obtained on a relatively short column (see Fig. 1). Probably, a total resolution could be obtained by the recycling technique of Porath and Bennich [7]. A practical example is given in Fig. 2 showing the purification of hydroxymethylferrocene, which was obtained from a commercial supplier as a sample of nonspecified purity. Reference samples were prepared either from (ferrocenylmethyl)trimethylammonium iodide and sodium hydroxide, or by reduction of formylferrocene with sodium borohydride in methanol. Both ferrocene and α-hydroxyethylferrocene were detected in the commercial product. Also, commercial formylferrocene yielded a reduction product which contained considerable amounts of α-hydroxyethylferrocene besides the main component, hydroxymethylferrocene.

Mechanism of separation

Our experiments were carried out at room temperature and atmospheric pressure. We have not yet obtained sufficient data concerning the influence of different physical parameters like temperature, pressure, and flow rate upon the distribution constants of the organometallic solutes and therefore cannot present a detailed model of the separation mechanism. Since all K_{av}-values are larger than 1.0 it may be inferred that the separations achieved in the system X2—cyclohexane are due to weak interactions between solute and gel matrix and not by a molecular sieving process (which would be characterized by K_{av} between 0 and 1.0). This idea is further supported by the separation of the

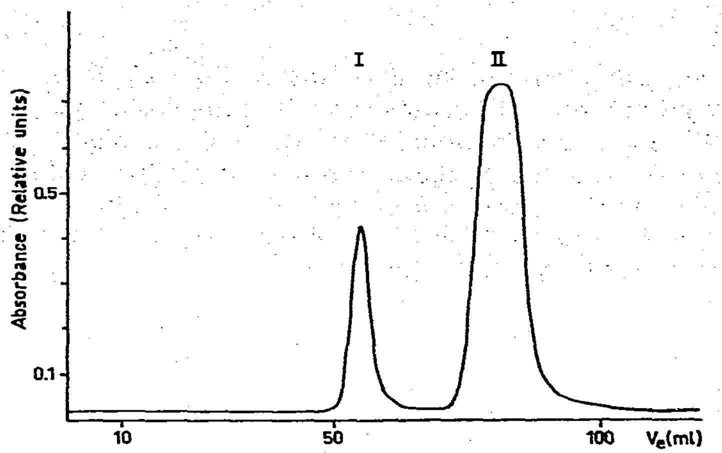

Fig. 3. Separation of *trans*-azobenzene and 4-dimethylaminoazobenzene on X2—cyclohexane. For column dimensions, see Table 1.

dicyclopentadienyl complexes of iron, ruthenium, and osmium, which possess nearly equal molar volumes (see ref. 4, p. 33) and thus would be expected to migrate equally fast in a molecular sieving system where no interaction between solute and matrix occurs. Hereby, we neglect the possible contribution of solvation to the effective molar volume of the dissolved species assuming that the metallocene would be (if at all) very weakly solvated by cyclohexane. The weakness of the interaction is also indicated by the symmetry of the elution peaks of all of the metallocene derivatives tested so far, in contrast to the behaviour of azo dyes, where some tailing could be observed (see Fig. 3). The pore size of the network is nevertheless a critical factor in these interactions as is shown by comparison of X2 and X8 in the same solvent, cyclohexane. The latter polymer showed negligible swelling; all organometallics were eluted with the void volume. We believe that our separations will fit a partition model rather than an adsorption model (see ref. 5, p. 85), but the number and relative importance of the physical parameters involved remains yet to be determined.

From a practical point of view, the system X2—cyclohexane is advantageous in various respects: (i) it is chemically inert both in concern of the matrix and the solvent and could therefore be used where polar matrices or solvents could lead to reaction with the solutes, or where molecular rearrangements are induced by polar media [8]; (ii) the material consisting of spherical beads provides high flow rates at normal pressure and is ready for use again when the last component has passed the column. Sometimes we have found coloured material to adsorb strongly on the gels; they could in most instances be desorbed by washing with highly polar solvents, e.g. dimethylformamide. This of course necessitates elimination of the particular solvent by washing with a third, volatile solvent, subsequent drying and repacking of the column in cyclohexane; (iii) cyclohexane is easily purified and does not give rise to the formation of peroxides.

A drawback in certain cases may be the moderate solubility of some organometallic compounds in this solvent at normal temperature and pressure. The system X2—cyclohexane may be useful for the separation of other classes of compounds (see Fig. 3).

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