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ELUTION BEHAVIOUR OF SOME DERIVATIVES OF 2-(4-HYDROXYPHENYL)-2-PHENYLPROPANE ON SEPHADEX LH-20 IN METHANOL AND N,N-DIMETHYLFORMAMIDE

B. I. SHOPOVA, I. T. MLADENOV and K. S. KURTEV
Higher Institute of Chemical Technology "Professor Dr. A. Zlatarov", Bourgas (Bulgaria)
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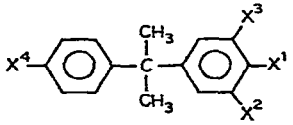
SUMMARY

The elution behaviour of some derivatives of 2-(4-hydroxyphenyl)-2-phenylpropane (cumylphenol) on Sephadex LH-20 in methanol and N,N-dimethylformamide has been studied. In methanol, all of the compounds are adsorbed on the gel, through π-bonding and hydrogen bonding. In N,N-dimethylformamide, the derivatives in which the hydroxyl group is free or substituted by an amino group partially permeate the gel, while those in which the hydroxyl group is substituted by chlorine or is methylated are completely excluded. Some of the cumylphenol derivatives can be successfully separated both in methanol and in N,N-dimethylformamide.

INTRODUCTION

Recently[1] a number of new derivatives of 2-(4-hydroxyphenyl)-2-phenylpropane (cumylphenol) have been synthesized, their common formula being:



in which X^1 = OH, OCH_3, OC_2H_5, Cl or NH_2; X^2 and X^3 = NO_2, NH_2 or H; and X^4 = H or NO_2. Since these compounds are prepared from each other, it is necessary to device methods of separating their mixtures. As Sotobayashi *et al.*[2], Brook and Munday[3], Streuli[4,5] and Berek and Bakoš[6] have shown, chromatography on Sephadex LH-20, with a suitable eluent, offers interesting possibilities for the separation of aromatic compounds possessing different functional groups.

The present work was undertaken in order to examine the elution behaviour of cumylphenol and some of its derivatives on Sephadex LH-20 with different eluents. The results help to draw some conclusions as to the possibility of separating pairs of cumylphenol derivatives obtained in succession. Also, from a theoretical point of view, the interaction of these polyfunctional aromatic compounds with Sephadex LH-20 in various solvents is of interest, since the interactions may be predicted from

the known information on this gel. This paper gives the results for elution with methanol and N,N-dimethylformamide. Experiments with acetone and 1,4-dioxan are in progress.

EXPERIMENTAL

Cumylphenol was isolated by means of vacuum distillation from phenol resin, a by-product of the production of phenol and acetone by the cumene method. The remaining compounds were obtained from reactions of cumylphenol or its derivatives[1]. Before the experiments, all of the compounds were refined by repeated crystallization to a constant melting point.

The experiments were carried in two glass columns of the same diameter and filled with Sephadex LH-20 swelled in methanol or N,N-dimethylformamide (DMFA). The main characteristics of the gel bed and some experimental conditions are given in Table I.

TABLE I

COLUMN CHARACTERISTICS AND EXPERIMENTAL CONDITIONS

Eluent	*Methanol*	*DMFA*
Column diameter (cm)	2.7	2.7
Height of gel bed (cm)	47.7	47.6
Dry weight of gel (g)	65	64
Total volume of gel bed, V_t (ml)	273	272
Void volume, V_0 (ml)	103	92
Inner volume, V_i (ml)	123.5	141
Sample size (mg)	5	5
Sample volume (ml)	0.7	0.7
Flow-rate (ml/h)	60	60

A constant flow-rate was maintained by means of a Mariotte bottle. The eluate was collected by an automatic collector. The volume of the eluate (V_e) was checked by use of a graduated cylinder having a precision of $\pm$ 0.05 ml. An Abbé refractometer was employed as a detector. In the elution region of the compounds, the refractive index of each millilitre of the eluate was measured. At least three values of the elution volume were obtained for each compound. Elution volumes were reproducible to $\pm$1 ml. The void volumes (V_0) were determined using a 0.5% aqueous solution of Blue Dextran 2000 (for the methanol column) and polystyrene (for the DMFA column). The inner volumes (V_i) were calculated as the product of the corresponding solvent regain (manufacturer's values[7]) and the dry weight of the gel. Values of the distribution coefficient (K_D) were calculated from the standard equation: $K_D = (V_e - V_0)/V_i$.

RESULTS AND DISCUSSION

K_D Values of cumylphenol and its derivatives from their elution on Sephadex LH-20 in methanol and DMFA are listed in Table II.

TABLE II

K_D VALUES OF CUMYLPHENOL AND ITS DERIVATIVES ON SEPHADEX LH-20 IN METHANOL AND DMFA

No.	*Cumylphenol derivative*	*Eluting medium*	
		Methanol	*DMFA*
I	2-(4-Hydroxyphenyl)-2-phenylpropane(cumylphenol)	1.39	0.57
II	2-(4-Hydroxy-3-nitrophenyl)-2-phenylpropane (mononitrocumylphenol)	1.41	0.56
III	2-(4-Hydroxy-3,5-dinitrophenyl)-2-phenylpropane (dinitrocumylphenol)	1.83	0.55
IV	2-(4-Hydroxy-3,5-dinitrophenyl)-2-(4'-nitrophenyl) propane (trinitrocumylphenol)	1.98	0.53
V	2-(4-Ethoxy-3-nitrophenyl)-2-phenylpropane	1.40	0.54
VI	2-(4-Methoxy-3,5-dinitrophenyl)-2-phenylpropane	1.19	0.04
VII	2-(4-Methoxy-3,5-dinitrophenyl)-2-(4'-nitrophenyl)propane	1.16	0.01
VIII	2-(4-Chloro-3,5-dinitrophenyl)-2-phenylpropane	1.27	0.05
IX	2-(4-Chloro-3,5-dinitrophenyl)-2-(4'-nitrophenyl)propane	1.19	0.03
X	2-(3-Amino-4-hydroxy-5-nitrophenyl)-2-phenylpropane	1.83	0.55
XI	2-(4-Amino-3,5-dinitrophenyl)-2-phenylpropane	1.58	0.55
XII	2-(4-Amino-3,5-dinitrophenyl)-2-(4'-nitrophenyl)propane	1.74	0.49

Elution behaviour in methanol

According to Streuli[5], when aromatic compounds are eluted on Sephadex LH-20 in methanol the predominant interaction is π-bonding, but some compounds also interact further with the gel by hydrogen bonding.

Our results obtained from the elution of cumylphenol derivatives confirm these conclusions. All of the compounds were adsorbed on the gel by π-bonding, since their K_D values were greater than 1.0. However, cumylphenol derivatives in which the hydroxyl group was not substituted, had higher K_D values than those in which the hydroxyl group was substituted by chlorine or was methylated.

An inspection of K_D values for cumylphenol (I), mononitrocumylphenol (II), dinitrocumylphenol (III) and trinitrocumylphenol (IV) shows that elution takes place contrary to the sieving mechanism. Obviously, cumylphenol exhibits further interaction with the gel by means of hydrogen bonding through the hydroxyl group and this interaction becomes stronger with the successive addition of nitro groups to its molecule. The K_D value becomes especially high when the second nitro group is added *ortho* to the hydroxyl group. These facts are adequately explained in terms of the fact that nitrophenols are stronger acids than phenol because of the additional protonisation of the hydrogen atom in the hydroxyl group. Brook and Munday[3] studied the elution behaviour of *m*- and *p*-nitrophenol on Sephadex LH-20 in buffer solution and showed that these compounds are more strongly adsorbed than phenol. Streuli's[5] K_D value for 3-nitrophenol on Sephadex LH-20 in methanol is higher than that for phenol.

The K_D values are also high for cumylphenol derivatives XI and XII (Tabel II), in which the hydroxyl group is substituted by an amino group. These results indicate that the amino group also takes part in the formation of hydrogen bonds with the gel, but not so strongly as the hydroxyl group since the K_D values for compounds XI and XII are lower than those of III and IV. In this case too, addition of another nitro

group in its *para* position of the second benzene ring strengthens the interaction with the gel.

The K_D value for X, which contains both an amino and a hydroxyl group, is the same as that for III. Obviously steric hindrance prevents the formation of hydrogen bonding simultaneously through the hydroxyl and amino groups.

The compounds that are retarded only through π-bonding with the gel show a very slight sieving mechanism. To demonstrate this we can compare K_D values for VIII with those for IX on the one hand, and K_D values for VI with those for VII (methyl ethers of di- and trinitrocumylphenol) on the other.

The behaviour of V (ethyl ether of mononitrocumylphenol) is of interest since its K_D value is considerably higher than those for VI and VII and is very close to that for II. The only possible explanation of this fact is that the ether oxygen atom of V also takes part in the formation of hydrogen bonds with the gel, where the proton donors are the residual hydroxyl groups of Sephadex LH-20. This interaction is not possible with the ethers of VI and VII because of the steric hindrance of the two nitro groups.

Elution behaviour in DMFA

From Table II it can be seen that, for all of the compounds, $K_D < 1$. This indicates that none of the compounds is adsorbed. Therefore in DMFA there is no π-bonding between the solutes and the gel, as was also shown by Streuli[5] for other aromatic compounds. Moreover, none of cumylphenol derivatives freely permeates the gel. Most of them only partially permeate the gel phase ($0 < K_D < 0.8$). Compounds in which the hydroxyl group is methylated or substituted by chlorine are completely excluded ($K_D \approx 0$). In DMFA the large molecules of the solutes are probably surrounded by a thick solvate layer, which causes their partial or complete exclusion from the pores of the gel.

Streuli[5] and Berek and Bakoš[6] observed a hydrogen-bonding interaction in DMFA between some compounds and Sephadex LH-20. Although cumylphenol derivatives do not show adsorbtion on this gel in DMFA, there was a tendency for some of these compounds to interact with the gel by means of hydrogen bonding, as also occurred in methanol. The compounds were those in which the hydroxyl group was not substituted or which was substituted by an amino group, and which permeate,

TABLE III

SEPARATION VOLUMES OF SOME PAIRS OF CUMYLPHENOL DERIVATIVES ON SEPHADEX LH-20 IN METHANOL AND DMFA

Pair of derivatives	*Separation volume, V_s (cm^3)*		*Pair of derivatives*	*Separation volume, V_s (cm^3)*	
	Methanol	*DMFA*		*Methanol*	*DMFA*
I, II	2	1	XI, VI	48	72
V, II	1	3	X, III	0	0
II, III	52	1	IX, IV	98	71
VI, III	79	72	IV, XII	101	73
VIII, III	69	73	IX, XII	68	75
VI, VIII	10	1	VII, XII	72	68
XI, VIII	38	73			

although only partially, the gel. The ethyl ether of mononitrocumylphenol (V), which in methanol forms hydrogen bonds with Sephadex LH-20, partially permeates the gel in DMFA, while the methyl ethers of di- and tri-nitrocumylphenol (VI and VII) are almost completely excluded.

The possibilities of separating some pairs of cumylphenol derivatives obtained in succession

For the point of view of the synthesis of cumylphenol derivatives, it is interesting to consider the possibility of separating the 13 pairs of these compounds. In Table III the separation volumes (V_S) of these pairs are listed [$V_S = (K'_D - K''_D) \cdot V_i$] in methanol and in DMFA. Bearing in mind the fact that the maximum peak width in our experiments was 19 cm^3 in methanol and 15 cm^3 in DMFA, it is clear that 9 of these pairs can be well separated in methanol and 8 in DMFA.

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