

Preparation and properties of 1-[4-(2-alkoxyphenoxy)butyl]- and 1-[4-(3-alkoxyphenoxy)butyl]-1-ethylpiperidinium bromides

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The synthesis of 1-[4-(2-alkoxyphenoxy)butyl]- and 1-[4-(3-alkoxyphenoxy)butyl]-1-ethylpiperidinium bromides and their ultraviolet and infrared spectra are described.

Описывается синтез, УФ и ИК спектры 1-[4-(2-алкоксифенокс)бутил]- и 1-[4-(3-алкоксифенокс)бутил]-1-этилпиперидиниевых бромидов.

Studying the mechanism of solubilization of organic compounds in water [1] we presented in our previous work [2] a series of ammonium salts of the type 1-[4-(4-alkoxyphenoxy)butyl]-1-ethylpiperidinium bromides as model solubilization agents. Some of these compounds exhibited a considerable antibacterial activity. To follow the microbiological activity of the presented type of organic ammonium salts in dependence on the position of the alkoxy on benzene ring [3] it was necessary to prepare further positional isomers. It was shown that from *p*-alkoxy substituted organic ammonium salts hexyloxy and heptyloxy derivatives were the most active ones. Therefore, in the present work we focussed our attention on the preparation of their *o*- and *m*-positional isomers.

Experimental

The starting *o*- and *m*-alkoxyphenols were obtained according to [4, 5], 2- and 3-alkoxyphenoxybutyl bromides were prepared by a modified method of Marvel [6]. The final ammonium salts were prepared similarly as in [2]. The model compound for the study of u.v. and i.r. spectra — 1,3-dimethoxybenzene — was prepared by methylation of resorcinol with dimethyl sulfate [4].

Infrared spectra of 0.2 M solutions of the compounds in CHCl_3 , anal. grade, and CDCl_3 (99.95%) were taken in NaCl cells of 0.044, 0.068, and 0.108 mm thickness on a double-beam UR-20 instrument (Zeiss, Jena) in the 4000–670 cm^{-1} region. Methanol and moisture were removed from CHCl_3 before use by passing it through a column filled with silica gel. Some of the compounds were measured also in KBr pellets or neat. Polystyrene foil was used for calibration. The wavenumber reading accuracy was $\pm 1 \text{ cm}^{-1}$. The spectral data of $\nu_{\text{as}}(\text{C}_{\text{ar}}-\text{O}-\text{C})$ presented in Table 4 are the average of the values obtained from three records at stabilized current voltage 220 V.

Ultraviolet spectra were measured on a Specord UV VIS spectrophotometer (Zeiss, Jena) in 1×10^{-4} M ethanolic solutions by using 1-cm silica cells. The accuracy of measurements was $\pm 1 \text{ nm}$.

Results and discussion

2-Alkoxyphenols presented in Table 1 were prepared by the reaction of pyrocatechol with equimolar quantities of alkyl bromide and potassium hydroxide in aqueous-alcoholic medium. The low yields (*ortho* effect) are in line with the literature data [5].

Table 1

Characterization of 2-alkoxyphenols

No.	R	Formula	M_r	Calculated/found		Yield %	B.p. °C/Pa
				% C	% H		
I	2-Hexyl	$\text{C}_{12}\text{H}_{18}\text{O}_2$	194.27	74.09	9.26	28	106/120
				73.78	9.37		
II	2-Heptyl	$\text{C}_{13}\text{H}_{20}\text{O}_2$	208.36	74.87	9.59	32	118/26
				75.50	10.20		

2-Alkoxyphenoxybutyl bromides and 3-alkoxyphenoxybutyl bromides (Table 2) were prepared by the reaction of 0.3 molar excess of 1,4-dibromobutane with the appropriate alkoxyphenol and 0.2 molar excess of sodium hydroxide in aqueous medium. The method of Marvel [6] was modified by the way of isolation of the product from the reaction mixture. The isolation of the final product was accomplished by extraction with toluene and subsequent fractional distillation under reduced pressure.

1-[4-(2-Alkoxyphenoxy)butyl]- and 1-[4-(3-alkoxyphenoxy)butyl]-1-ethylpyperidinium bromides (Table 3) were prepared by the reaction of 1-ethyl-

Table 2

Characterization of 2- and 3-alkoxyphenoxybutyl bromides

No.	R	Formula	M_r	Calculated/found		Yield %	B.p. °C/Pa
				% C	% H		
III	2-Hexyl	$C_{16}H_{25}BrO_2$	329.29	58.30	7.59	49	158—161/16
				58.46	7.60		
IV	2-Heptyl	$C_{17}H_{27}BrO_2$	343.31	59.42	7.86	44	168/66
				59.56	7.79		
V	3-Hexyl	$C_{16}H_{25}BrO_2$	329.29	58.30	7.59	50	187/186
				58.41	7.62		
VI	3-Heptyl	$C_{17}H_{27}BrO_2$	343.31	59.42	7.86	50	184/160
				59.51	7.91		

Table 3

Characterization of 1-[4-(2-alkoxyphenoxy)butyl]- and 1-[4-(3-alkoxyphenoxy)butyl]-1-ethylpiperidinium bromides

No.	R	Formula	M_r	Calculated/found			Yield %	M.p., °C (Kofler)
				% C	% H	% N		
VII	2-Hexyl	$C_{23}H_{40}BrNO_2$	442.50	62.43	9.11	3.16	85	74—75
				62.82	9.05	3.27		
VIII	2-Heptyl	$C_{24}H_{42}BrNO_2$	456.52	63.14	9.27	3.07	88	38—40
				62.85	9.28	3.25		
IX	3-Hexyl	$C_{23}H_{40}BrNO_2$	442.50	62.43	9.11	3.16	84	77—79
				62.76	9.30	3.18		
X	3-Heptyl	$C_{24}H_{42}BrNO_2$	456.52	63.14	9.27	3.07	81	49—50
				63.51	9.50	2.92		

piperidine with 2- and 3-alkoxyphenoxybutyl bromides, respectively, in anhydrous ethanol [2]. The obtained organic ammonium salts were white crystalline hygroscopic compounds. This property caused difficulties in the isolation of crystalline products from the solution. All the compounds presented in Tables 1—3 were hitherto not described.

In the i.r. spectra of the investigated compounds we focussed our attention on the $C_{ar}-O-C$ ether linkage. Some authors [7—9] reported that the alkoxy group on the aromatic ring usually caused a formation of two bands suitable for correlation in the region 1310—1210 and 1050—1010 cm^{-1} . The absorption band belonging to $C_{ar}-O-C$ in *meta* position appeared at higher wavenumber than that belonging to $C_{ar}-O-C$ in the *ortho* and *para* positions, respectively [10]. On the basis of

Table 4

Spectral data of the prepared 1-[4-(2-alkoxyphenoxy)butyl]- and 1-[4-(3-alkoxyphenoxy)butyl]-1-ethylpiperidinium bromides

No.	Isomer	Ultraviolet spectra						Infrared spectra $\nu_{as}(C_{ar}-O-C)$		
		λ_{max} nm	$\log \epsilon$	λ'_{max} nm	$\log \epsilon$	λ''_{max} nm	$\log \epsilon$	$\tilde{\nu}$ cm^{-1}	$\Delta\tilde{\nu} a^{1/2}$ cm^{-1}	ϵ^a $M^{-1} cm^{-1}$
VII	<i>o</i> -	225	3.86	277	3.40	282 sh	3.33	1252 ^a	24 ^a	520 ^a
VIII	<i>o</i> -	225	3.89	277	3.41	282 sh	3.32	1252 ^a	24 ^a	600 ^a
IX	<i>m</i> -	221	3.88	274	3.34	279	3.30	1284 ^b	23 ^b	203 ^b
								1286 ^c	19 ^c	—
X	<i>m</i> -	221	3.85	274	3.33	279	3.29	1286 ^b	24 ^b	192 ^b
								1289 ^c	26 ^c	—
XI ^f	<i>m</i> -	221	3.88	274	3.34	279	3.30	1290 ^c	23 ^c	—
XII ^d	<i>p</i> -	228	4.03	292	3.42	298 sh	3.36	1233 ^a	21 ^a	671 ^a
XIII ^d	<i>p</i> -	228	4.02	292	3.38	298 sh	3.33	1232 ^a	20 ^a	653 ^a

a) In $CHCl_3$; b) in $CDCl_3$; c) in KBr; d) data from [2]; e) in the original state as a liquid; f) XI — model compound 1,3-dimethoxybenzene; sh — shoulder.

the above knowledge, we studied in the i.r. spectra the absorption region of the $C_{ar}-O-C$ ether linkage belonging to asymmetrical stretching vibrations. The compounds having two $C_{ar}-O-C$ bonds in the *ortho* or *para* positions on benzene ring showed one intensive band at 1250 and 1230 cm^{-1} , respectively ([2]; see Table 4). Regarding the intensities of the absorption bands, the *meta* substituted derivatives differed very much from the original unsubstituted compound — 1-(phenoxybutyl)-1-ethylpiperidinium bromide — as well as from the *ortho* and *para* substituted derivatives. To locate precisely the absorption bands of asymmetrical stretching vibrations of the ether linkage on the aromatic ring in the spectral range 1300—1200 cm^{-1} , it was necessary to carry out measurements in KBr pellets and in $CDCl_3$ solutions. From this study followed that contrary to *ortho* and *para* derivatives, the *meta* derivative had two bands in KBr as well as in $CDCl_3$ solution and three bands in $CHCl_3$ solution. The absorption band of $\nu_{as}(C_{ar}-O-C)$ was split into two strong absorption bands (doublet almost of the same intensity at 1290—1268 cm^{-1} denoted as XI in Table 4) also in the case of the model compound (1,3-dimethoxybenzene). The i.r. spectral data are presented only for the more intense absorption band at 1290 cm^{-1} with all *m*-derivatives in solid state as well as in $CDCl_3$ solutions (Table 4). The values of the effective molar absorption coefficients and half-band width of bands of *m*-derivatives differed a little each from the other. Comparison of *m*-derivatives with the *o*- and *p*-derivatives showed that the greatest differences were in the wavenumbers and intensities of bands, which was in agreement with the literature data [10]. Besides, we found characteristic absorption bands at 690 and 770 cm^{-1} confirming the *m*-position of the alkoxy group similarly as in our previous work [2]; with *p*-derivatives these bands appeared at 825 cm^{-1} . The above-mentioned bands were ascribed to out-of-plane wagging vibrations of adjacent hydrogen atoms on the aromatic ring.

Ultraviolet spectra proved that the *ortho*, *meta*, and *para* disubstituted derivatives of benzene were characterized by two main absorption bands. The wavenumber and intensity of the bands indicated that mesomeric and steric effects were involved [11]. These absorption bands corresponded to 1L_a and 1L_b bands of the unsubstituted benzene [12].

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