Synthesis, u.v. and i.r. spectra of 2-piperidinoethyl esters of alkyloxyphenylcarbamic acids

J. ČIŽMÁRIK and A. BOROVANSKÝ

*Department of Pharmaceutical Chemistry, Faculty of Pharmacy,
Komenský University, 880 34 Bratislava*

The preparation of hydrochlorides of thirty homologous 2-piperidinoethyl esters of alkyloxyphenylcarbamic acids is described together with their i.r. and u.v. spectra. The results of spectral measurements are discussed in more detail.

Various types of basic esters of alkyloxyphenylcarbamic acids were studied in several previous works [1—5]. The esters were prepared by usual procedure, *i.e.* by addition of basic aminoalcohol on alkyloxyphenyl isocyanate in the medium of inert anhydrous solvent, toluene or benzene as a rule. Pharmacological tests showed high local-anaesthetic activity of a number of the prepared compounds.

Continuing the systematic studies of this type of compounds, we prepared a series of 2-piperidinoethyl esters of alkyloxyphenylcarbamic acids (from methoxy to decyloxy derivatives) and studied their spectral parameters in the u.v. and i.r. region. The preparation was based on the procedure described by *Borovanský et al.* [4] consisting in alkylation of 2-, 3-, and 4-acetaminophenols from which the corresponding alkyloxyanilines were prepared. These were converted into corresponding alkyloxyphenyl isocyanates by reaction with phosgene. The final products were obtained by heating alkyloxyphenyl isocyanates with 2-piperidinoethanol in the medium of anhydrous toluene. The obtained basic esters were isolated and identified in the form of hydrochlorides.

Experimental

Melting points were determined on a Kofler microstage. The prepared substances are characterized in Table 1.

The i.r. spectra of the prepared compounds *I—XXX* were measured with a UR-20 (Zeiss, Jena) spectrophotometer in the region $500—3800 \ cm^{-1}$, using 0.02 M chloroform solutions in cells with $d = 1$ mm. Calibration was done with a standard polystyrene foil. The wavenumber reading accuracy was $\pm 1 \ cm^{-1}$.

The u.v. spectra (200—320 nm) were measured by a PYE UNICAM SP 1800 B spectrophotometer with a linear recorder AR, in 1-cm quartz cells. Concentrations of the used aqueous solutions were 1×10^{-4} M for 2-substituted derivatives and 5×10^{-5} M for 3- and 4-substituted derivatives. The recorded u.v. spectra were resolved into individual bands according to the method of *Jaffé* and *Orchin* [6]. The results of spectral measurements together with the derived parameters are listed in Table 2.

Table 1

Characterization of the prepared compounds

$$NH-COO-CH_2-CH_2\overset{+}{N}\!\!\!\diagup\!\!\!\searrow$$ ... OR ... Cl⁻
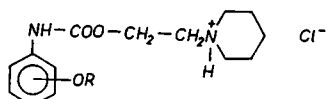
Com-pound	R	Formula	M	Calculated/found			Yield [%]	M.p. [°C]
				% C	% H	% N		
I	2-CH₃	C₁₅H₂₃N₂O₃Cl	314.79	57.23	7.36	8.89	82	151—153ᵃ
				57.30	7.68	8.85		
II	·3-CH₃	C₁₅H₂₃N₂O₃Cl	314.79	57.23	7.36	8.89	88	170—172ᵃ
				57.38	7.43	8.99		
III	4-CH₃	C₁₅H₂₃N₂O₃Cl	314.79	57.23	7.36	8.89	92	193—196ᵃ
				57.31	7.40	8.85		
IV	2-C₂H₅	C₁₆H₂₅N₂O₃Cl	328.81	58.44	7.66	8.51	86	155—157ᵃ
				58.22	7.80	8.47		
V	3-C₂H₅	C₁₆H₂₅N₂O₃Cl	328.81	58.44	7.66	8.51	88	193—195ᵃ
				58.65	7.78	8.50		
VI	4-C₂H₅	C₁₆H₂₅N₂O₃Cl	328.81	58.44	7.66	8.51	82	203—205ᵃ
				58.25	7.23	8.72		
VII	2-C₃H₇	C₁₇H₂₇N₂O₃Cl	342.84	59.56	7.98	8.17	96	136—138ᵇ
				59.27	7.76	8.15		
VIII	3-C₃H₇	C₁₇H₂₇N₂O₃Cl	342.84	59.56	7.98	8.17	70	188—190ᵇ
				59.40	7.42	8.40		
IX	4-C₃H₇	C₁₇H₂₇N₂O₃Cl	342.84	59.56	7.98	8.17	90	194—196ᵇ
				59.80	8.17	8.22		
X	2-C₄H₉	C₁₈H₂₉N₂O₃Cl	356.88	60.58	8.19	7.84	89	140—142ᵇ
				60.46	8.25	7.78		
XI	3-C₄H₉	C₁₈H₂₉N₂O₃Cl	356.88	60.58	8.19	7.84	40	183—185ᵇ
				60.26	8.33	8.01		
XII	4-C₄H₉	C₁₈H₂₉N₂O₃Cl	356.88	60.58	8.19	7.84	86	199—202ᵇ
				60.50	8.09	7.89		
XIII	2-C₅H₁₁	C₁₉H₃₁N₂O₃Cl	370.89	61.53	8.42	7.55	88	142—144ᵇ
				61.20	8.54	7.58		
XIV	3-C₅H₁₁	C₁₉H₃₁N₂O₃Cl	370.89	61.53	8.42	7.55	89	186—188ᵇ
				61.88	8.40	7.73		
XV	4-C₅H₁₁	C₁₉H₃₁N₂O₃Cl	370.89	61.53	8.42	7.55	94	193—195ᵇ
				61.70	8.54	7.56		
XVI	2-C₆H₁₃	C₂₀H₃₃N₂O₃Cl	384.95	62.40	8.64	7.27	78	131—133ᶜ
				62.46	8.61	7.07		
XVII	3-C₆H₁₃	C₂₀H₃₃N₂O₃Cl	384.95	62.40	8.64	7.27	85	179—181ᵇ
				62.67	8.54	7.05		
XVIII	4-C₆H₁₃	C₂₀H₃₃N₂O₃Cl	384.95	62.40	8.64	7.27	83	190—192ᵇ
				62.33	8.65	7.13		
XIX	2-C₇H₁₅	C₂₁H₃₅N₂O₃Cl	398.98	63.22	8.84	7.02	92	118—121ᶜ
				63.17	8.80	6.92		
XX	3-C₇H₁₅	C₂₁H₃₅N₂O₃Cl	398.98	63.22	8.84	7.02	90	176—178ᵇ
				63.04	8.89	6.85		
XXI	4-C₇H₁₅	C₂₁H₃₅N₂O₃Cl	398.98	63.22	8.84	7.02	82	184—185ᵇ
				63.20	8.79	7.00		
XXII	2-C₈H₁₇	C₂₂H₃₇N₂O₃Cl	413.50	63.90	9.01	6.77	50	124—125ᶜ
				63.64	9.00	6.95		
XXIII	3-C₈H₁₇	C₂₂H₃₇N₂O₃Cl	413.50	63.90	9.01	6.77	80	150—152ᵇ
				63.90	9.17	6.57		

Table 1 (Continued)

Com-pound	R	Formula	M	Calculated/found % C	% H	% N	Yield [%]	M.p. [°C]
XXIV	4-C_8H_{17}	$C_{22}H_{37}N_2O_3Cl$	413.50	63.90	9.01	6.77	72	170—173[b]
				63.75	9.02	6.75		
XXV	2-C_9H_{19}	$C_{23}H_{39}N_2O_3Cl$	427.03	64.69	9.20	6.56	28	128—130[c]
				64.54	9.48	6.68		
XXVI	3-C_9H_{19}	$C_{23}H_{39}N_2O_3Cl$	427.03	64.69	9.20	6.56	60	174—177[b]
				64.47	9.61	6.32		
XXVII	4-C_9H_{19}	$C_{23}H_{39}N_2O_3Cl$	427.03	64.69	9.20	6.56	77	178—179[b]
				64.60	9.15	6.60		
XXVIII	2-$C_{10}H_{21}$	$C_{24}H_{41}N_2O_3Cl$	441.06	65.35	9.37	6.35	51	124—126[c]
				65.32	9.49	6.29		
XXIX	3-$C_{10}H_{21}$	$C_{24}H_{41}N_2O_3Cl$	441.06	65.35	9.37	6.35	92	176—178[b]
				65.20	9.55	6.22		
XXX	4-$C_{10}H_{21}$	$C_{24}H_{41}N_2O_3Cl$	441.06	65.35	9.37	6.35	96	180—181[b]
				65.40	9.30	6.46		

Crystallized from a) benzene—ethanol, b) ethyl acetate—ethanol, c) ethyl acetate.

Table 2

Electronic spectra (parameters of the CT band) and i.r. spectra of the prepared compounds

Com-pound	λ_{max} [nm]	$\log \varepsilon_{max}$	f	$D_{lf} \cdot 10^{17}$	$\cos^2 \Theta$	$\nu(C{=}O)$ [cm^{-1}]	$\nu(N{-}H)$ [cm^{-1}]
I	234	3.91	0.146	3.117	0.54112	1738	3426
II	235	4.03	0.191	4.095	—	1738	3432
III	237	4.14	0.281	6.076	—	1734	3435
IV	233	3.95	0.180	3.827	0.58577	1738	3426
V	236	4.04	0.187	4.027	—	1738	3432
VI	237	4.17	0.307	6.639	—	1734	3435
VII	233	3.92	0.174	3.699	0.54520	1738	3427
VIII	235	4.07	0.208	4.460	—	1737	3433
IX	237	4.18	0.306	6.617	—	1734	3435
X	232	3.93	0.181	3.831	0.56201	1738	3430
XI	236	4.05	0.195	4.199	—	1738	3433
XII	237	4.18	0.331	7.158	—	1734	3436
XIII	233	3.92	0.163	3.465	0.55098	1738	3430
XIV	235	4.05	0.214	4.589	—	1738	3433
XV	237	4.19	0.335	7.244	—	1734	3436
XVI	232	3.92	0.190	4.022	0.54909	1738	3430
XVII	235	4.05	0.197	4.224	—	1738	3434
XVIII	238	4.18	0.306	6.645	—	1734	3436
XIX	233	3.93	0.178	3.784	0.56430	1738	3430
XX	236	4.05	0.180	3.876	—	1738	3434
XXI	238	4.18	0.307	6.667	—	1734	3437
XXII	233	3.92	0.177	3.763	0.55431	1738	3429
XXIII	236	4.06	0.203	4.371	—	1738	3434
XXIV	238	4.18	0.305	6.623	—	1734	3437
XXV	233	3.93	0.169	3.593	0.55705	1738	3429
XXVI	236	3.98	0,178	3.833	—	1738	3434
XXVII	237	4.18	0.329	7.114	—	1734	3437
XXVIII	233	3.93	0.178	3.784	0.55738	1738	3429
XXIX	236	4.17	0.190	4.091	—	1738	3434
XXX	238	4.18	0.320	6.949	—	1734	3437

Discussion

Electronic spectra of the studied compounds show three characteristic bands in the region 190—300 nm. The so-called first local excitation band [7] has λ_{max} near to 280 nm, λ_{max} of the CT band is *ca.* 235 nm, and the second local excitation band has λ_{max} at about 205 nm. The CT band is most convenient for studying the substitution on the benzene ring because of its high sensitivity to the nature and position of a substituent. This was utilized also in our work and therefore the discussed relationships and physical parameters refer to the CT band.

For comparison purposes, the influence of the alkyloxy substituent on spectral parameters of the studied series, the spectra of the mother compound of this series were also measured under the above-described conditions. The mother compound, chloride of 2-piperidinoethyl phenylcarbamate, was originally synthesized by *Häring* [8]. We found $\lambda_{max} = 233$ nm, log $\varepsilon_{max} = 4.18$, $f = 0.295$, $D_{if} = 6.271 \times 10^{-17}$, $\cos^2 \Theta = 1$, *i.e.* $\Theta = 90°$ (CT band); from the i.r. spectrum $\nu(C=O) = 1741$ cm^{-1} and $\nu(N-H) = 3442$ cm^{-1}.

The following conclusions can be drawn from the analysis of the parameters of the u.v. spectra listed in Table 2.

In the triad of 2-, 3-, and 4-substituted derivatives, the λ_{max} values of the CT band increase gradually from 2- through 3- to 4-substituted derivatives. Values of λ_{max} of the CT band thus enable to identify the position of a substituent in this triad of derivatives.

The oscillator force f is a quantum-mechanical expression of the band intensity and also a parameter reflecting the extension (length) of the conjugated system. The highest f value of the 4-substituted derivatives is connected with the extended conjugation of the π bonds. The found f values confirmed the dependence of the absorption band intensity on the length of the conjugated system; the longer is the conjugated system, the greater is the band intensity and the oscillator force.

Since the oscillator force is a function of the integral absorbed energy, it is also one of the factors determining the dipole moment D_{if} of the electron transition. This quantity, expressing the transition moment of an electron on the excitation caused by the absorption of radiation, was calculated from a relationship derived by *Mulliken* [9]. In the series of the 2-, 3-, and 4-substituted derivatives, the D_{if} values are highest for the 4-isomers and they decrease through 3- to 2-isomers.

Values of $\cos^2 \Theta$ were calculated from the formula of *Braude* and *Sondheimer* [10]. The calculated values of Θ *i.e.* the angle of distortion of the plane of the benzene ring with respect to the carbamate plane, are practically independent of the number of carbons in the alkyloxy chain. The Θ value of the 2-methoxy derivative is practically equal to that of the 2-decyloxy derivative. The mean value for 2-alkyloxy derivatives is $\cos^2 \Theta = 0.55669$, *i.e.* $\Theta = 41°44'27''$

The C=O stretching frequency of the 2-substituted derivatives of alkyloxyphenylcarbamic acids is 1738 cm^{-1}; this value is practically independent of the length of the aliphatic chain of the alkoxy group. The N—H stretching vibrations of the 2-substituted derivatives are observed in the region 3430—3426 cm^{-1}, the frequencies varying only very slightly with lengthening of the alkoxy chain.

The C=O stretching frequency of the 3-substituted derivatives is *ca.* 1738 cm^{-1}, *i.e.* the same as the value of 2-isomers. A possible explanation is that the substituent in the position 2 or 3 influences in the same way the force constant of the bond in the benzene ring and consequently the frequency of the $>C=O$ group.

Lower $\nu(C{=}O)$ frequencies were observed with 4-substituted derivatives where +M effect might occur. In this position, the alkyloxy group exerts a substantially stronger influence upon the electron distribution in the benzene ring, owing to a possible shift towards the mesomeric structure (Scheme 1).
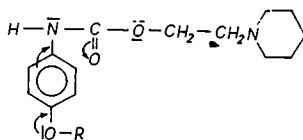
Scheme 1

The appearance of such a shift of electrons increases the probability of lengthening the π-bond conjugation which is little probable in the molecule of 2- and 3-substituted derivatives.

The frequency of the N—H stretching vibrations of 3-substituted derivatives is in the region 3434—3432 cm^{-1}, *i.e.* slightly higher than that of 2-substituted derivatives. Another slight increase of the $\nu(N{-}H)$ frequency was observed with 4-substituted derivatives (3437—3435 cm^{-1}). The frequency of the N—H stretching vibrations is more sensitive to the position of the substituent on the benzene ring. Lengthening of the aliphatic chain of the alkyloxy group brings about an increase of the frequency of the N—H stretching vibrations, observed for all the three position isomers (2-, 3-, and 4-). But the frequency of the C=O stretching vibration does not show such a trend.

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