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STRUCTURE OF PIPERIDINOETHYL ESTERS OF ALKOXYPHENYLCARBAMIC ACIDS AND THEIR THERMODYNAMIC PARAMETERS

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Abstract

The melting temperature of nine piperidinoethyl esters of alkoxyphenylcarbamic acid (hexaoxy-octyloxy) including all site isomers was investigated.

The analyses were performed using DSC apparatus, sample mass ranged from 0.2 to 2.5 mg, heating rate was 5 K min^{-1} and in static air atmosphere.

On the basis of melting peak, thermodynamic figures like: enthalpy, entropy, height and area of the peak and temperature of the partial peak were fixed.

For evaluation of the results Principal Component Analysis was applied. Thanks to this method the influence of length (mass) and position of alkoxy substituents on the thermodynamic parameters of melting of compounds under investigation were determined.

Keywords: DSC, melting peak, melting point, piperidinoethyl esters of alkoxyphenylcarbamic acid, principal component analysis

Introduction

Thermal method of analysis is widely used for investigation of the thermal decomposition of organic compounds [1–5]. These studies play an important role in the development of compounds, which are commonly used by manufacturers of drug, cosmetics, producers of the household chemistry and in industry of other chemical products.

Generally speaking, the thermal stability of organic compounds depends not only on the chemical structure but also on particle size, degree of crystallinity, the purity, temperature of storage and surrounding gas atmosphere and many other factors.

In this study one's attention was focused on investigation of relationship between position (on the ring of phenylcarbamic acid) alkoxy substituents and thermo-

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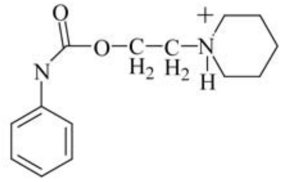
dynamic properties of components mentioned above. Studies melting point of chemical compounds are connected with the investigation on their thermal characteristics as a function of the temperature. These facts led to investigation on the melting point of nine piperidinoethyl esters of alkoxyphenylcarbamic acids (Table 1) in order to define the influence of chemical structure on their physical properties and additionally to obtain those thermal parameters which may be useful for defining their thermal stability and purity.

It was decided to test the foregoing in order to determine the influence of length of substituents and the places of their substitution on the thermodynamic parameters connected with the melting process of the nine newly synthesized esters revealing anaesthetic activity. The aim of mentioned above research was realized by using the Principal Component Analysis method. PCA is easy and comfortable to reduce the number of variables detecting structure in relationship between objects that is to classify compounds.

Table 1 Piperidinoethyl esters –2, –3, –4, ($O–C_{6–8}H_{13–17}$) substituted phenylcarbamic acid

Structure



Number of compounds	Substituent	Position *R*	Molecular mass
1	$O–C_6H_{13}$	2	384.95
2	$O–C_6H_{13}$	3	384.95
3	$O–C_6H_{13}$	4	384.95
4	$O–C_7H_{15}$	3	398.98
5	$O–C_7H_{15}$	4	398.98
6	$O–C_8H_{17}$	2	414.07
7	$O–C_8H_{17}$	3	414.07
8	$O–C_8H_{17}$	4	414.07
9	–	–	282.10

Experimental

Materials

In this study 2-piperidinoethyl esters of alkoxyphenylcarbamic acids were investigated (Table 1). This compounds were prepared in addition reaction after the scheme seen in Fig. 1. All the compounds used in testing were synthesized by Čižmárik and colleagues [3].

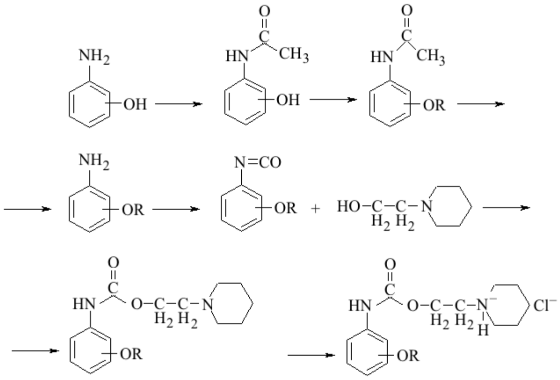


Fig. 1 The scheme of preparation of 2-piperidinoethyl esters of alkoxyphenylcarbamic acids

Thermal analysis

The DSC curves of melting of the studied compounds were carried out using DSC-2 Perkin Elmer (GB). The 0.2–2.5 mg samples were heated in copper crucible at heating rates 5 K min^{-1}. The analyses were performed in air atmosphere. As a reference Al_2O_3 was employed.

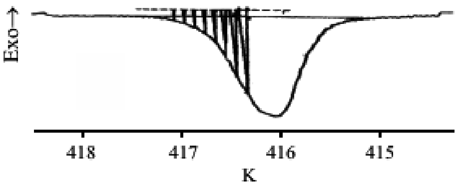


Fig. 2 Scheme of melting peak divided on equal segments formulated partial peaks

The interpretation of DSC curves consist of both kind of parameters: one kind obtained from whole melting peak, i.e. enthalpy, entropy, starting temperature, final temperature, melting point; and the second kind of parameters obtained after dividing peak on an equal segment (Fig. 2) like: area of partial peak, partial peak height and partial temperature.

Calculation

The Principal Component Analysis (PCA), an advanced statistical method were used for complex interpretation of experimental data [6–8, 10]. In this method high number of variables can be reduced to two or three principal components which very often illustrate relation among objects in multidimensional space.

The PCA consists of calculating of two new matrices: Principal Component Scores and Principal Component Loading according to experimental data set **X** with the dimension *np*, where *n* is a number of observation (rows) and *p* is a number of variables (columns). Principal Component Scores are set in matrix **P** with dimension *nk*, and Principal Component Loadings are contained in matrix **W** with dimension *pk* where *k* is a number of orthogonal principal components calculated for the given set. *K* does not exceed the number of *p* variables and as a rule is less than *p*. From the condition $k<p$ one can conclude, that the number of principal component is much less than number of experimental variables *p*.

Starting points for the calculation is matrix of the data **X**. In each of these matrices, nine piperidinoethyl esters of alkoxyphenylcarbamic acids were used as a row (*n*) which were called objects, whereas thermodynamically parameters of melting points of melting peaks like enthalpy, entropy, starting temperature of melt, partial temperature partial peak area were set as a column *p* and were called variables. Matrix **X** is a first standarized, then eigenvalues are calculated. Then it is need to estimate of how many factors to retain. By its nature this is an arbitrary decision. However there are some method commonly used in practice seem to yield the best results. In this case the screen test was used [11–14]. This is a method proposed by Cattell in 1966. Catell suggests to find place where the smooth decrease of eigenvalues appears [15] to level off to the right of the plot. To the right of this point, presumably, one find only 'factorial screen'. According to this criterion it would be probably retain 2 or 3 factors, which may be projected on two or three-dimensional plots. After further calculation, columns in matrices **P** and **W** were obtained, which were called principal components. New matrix **P** reflects main relation among objects and makes possible classification of the investigated samples, whereas matrix **W** illustrated main relation among variables and enables their selection.

In this study three matrices were constructed. While the first grouped data set contained whole thermodynamic parameters of melting peak, the second one consisted parameters of peak, which had not been divided to partial peak. In the third matrix only parameters calculated from divided (partial) peaks were used.

Results and discussion

Compounds 1–8 were subjected to the Principal Component Analysis. Three basic matrices were created on the base of the curves for each of samples tested from which every time the eigenvalues (Table 2) and two principal components were separated.

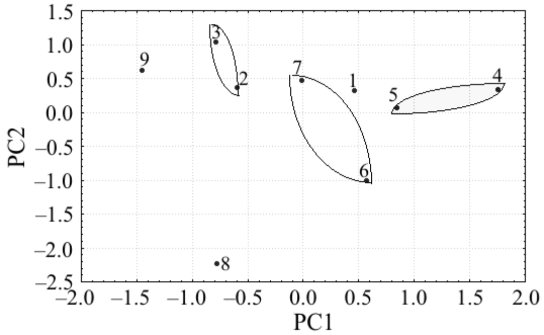


Fig. 3 Scatterplots of the first two Principal Component vectors (PC1 *vs*. PC2) for the first matrix

Table 2 Eigenvalues and percentage of variance

	Eigenvalue	Percentage of variance
1	10.58249	52.91
2	4.915218	24.58
3	6.918326	49.42
4	4.364185	31.17
5	3.986443	66.44
6	1.802033	30.03

The first matrix contained all thermodynamic data i.e. obtained from whole peaks as well as from divided peaks. The screen test showed that three principal components ought to be used to the construction of the graph, but, after constructing two- and three-dimensional graphs it was stated that two-dimensional graph presents relations better than three-dimensional (and that screen test should be applied cautiously). The values calculated from first matrix for all compounds have been placed in Table 2 (1–2).

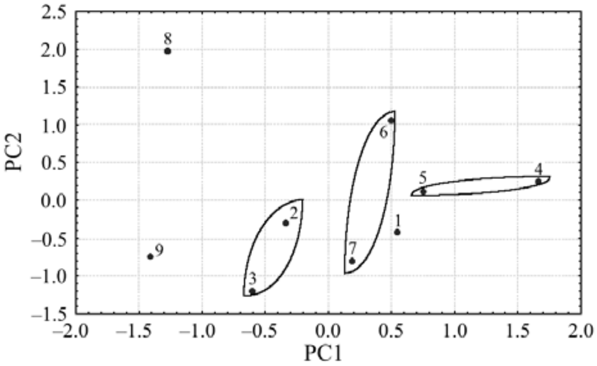


Fig. 4 Scatterplots of the first two Principal Component vectors (PC1 *vs*. PC2) for the second matrix

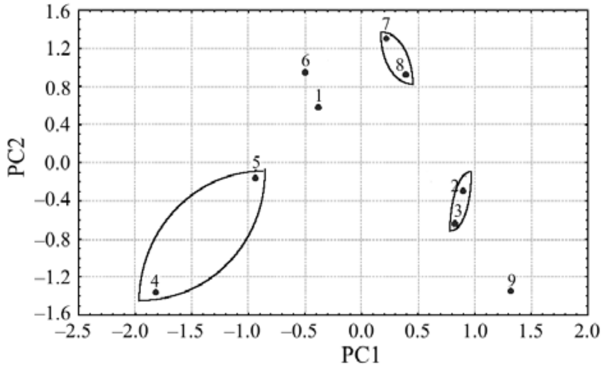


Fig. 5 Scatterplots of the first two Principal Component vectors (PC1 *vs*. PC2) for the third matrix

Second matrix contained only parameters of not divided peaks. In this case it was proceeded in the similar way, but only values of the first two principal components (PC1 and PC2) were considered. The eigenvalues of the principal components and percentage of their variance were shown in Table 2 (3–4). The values of principal components as a graphic illustration in form of scatter plot were shown on Fig. 4.

For the third matrix, in which the parameters of partial peaks created on the base of splitting the curves into equal segments were placed as variables, the first two principal components were also chosen and analogously as previously, were shown as a table and graph (Table 2 (5–6) and Fig. 5).

Conclusions

The results of the analysis showed that the melting parameters of individual samples depend, to a greater extent, on the length (mass) of alkoxy chain then on the places (position) of connection of this chain to the ring of the esters. Such a similarity takes place for isomers having the same length of alkoxy chain in the positions 3 and 4 of ester ring. The parameters of isomers substituted in the position 2 differ significantly from those substituted in position 3 as well as in position 4. Any relationship between thermodynamic properties of compounds substituted in the same position but with different chain length (from C_6–C_8) was not observed. The PCA carried out for esters including the substrate not substituted (labeled in Table 1 as 9) reveals its small similarity by the shortest chain substituted compounds in positions 3 and 4, although this similarity seems to be logical, it is hardly visible to state this unambiguously. However no correlation was revealed between heavier esters and not substituted esters.

References

1 G. W. H. Hohne, W. Hemminger and H. J. Flammersheim, Differential Scanning Calorimetry, Springer, New York 1996.
2 J. M. Rollinger and A. Burger, J. Therm. Anal. Cal., 68 (2002) 361.
3 P. Mura, P. Gratteri and M. T. Faucci, J. Therm. Anal. Cal., 68 (2002) 541.
4 D. Giron, J. Therm. Anal. Cal., 68 (2002) 335.
5 R. O. Macêdo, T. Gomes do Nascimento and J. W. E. Veras, J. Therm. Anal. Cal., 67 (2002) 483.
6 M. Wesołowski and T. Konarski, J. Therm. Anal. Cal., 55 (1999) 995.
7 M. Wesołowski, P. Konieczyński and B. Ulewicz, J. Therm. Anal. Cal., 66 (2000) 299.
8 M. Wesołowski, P. Konieczyński and B. Ulewicz-Magulska, J. Therm. Anal. Cal., 66 (2001) 593.
9 J. Čižmárik, A. Boravansky and P. Svec, Acta Facultatis Pharmaceuticae, 39 (1976) 53.
10 D. L. Massart, Fresenius Z. Anal. Chem., 305 (1981) 113.
11 L. Eriksson, L. Jonsson, M. Sjostrom and S. Wold, Quant. Struct. Act.-Relat., 7 (1988) 144.
12 R. E. Aries, D. P. Lidiard and R. A. Spragg, Chem. Brit., 9 (1991) 821.
13 Y. Darwish, T. Cserhati and E. Forgacs, Chem. Intel. Lab. Syst., 24 (1994) 169.
14 D. F. Morrison, Wielowymiarowa Analiza Statystyczna, PWN, Warszawa 1990.
15 J. C. Miller and J. N. Miller, Statistics for Analytical Chemistry, Wyd. 2, Ellis Horwood, London 1989.