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THERMAL DECOMPOSITION OF SILICON DERIVATIVES OF CINCHOCAINE

MAREK WESOŁOWSKI and JACEK TEODORCZYK

Analytical Chemistry Department and Inorganic Chemistry Department, Faculty of Pharmacy, Al. K. Marksa 107, PL 80-416 Gdańsk (Poland)

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ABSTRACT

Four silicon derivatives of the diethylaminoethyl amide of 2-butoxyquinoline-4-carboxylic acid (cinchocaine, nupercaine) have been thermally analysed. A very great similarity has been shown to exist in the decomposition of the derivatives, the mass-loss rate in the second decomposition stage of the methylsilyl derivatives of cinchocaine decreasing with the increase in the number of cinchocaine radicals in the compound examined. Owing to the low energy of the Si–N bond the volatile methylsilicon unit is liberated from the system without forming silicon dioxide as a residue. The analysis of the shape of peaks by Stoch's method has shown the endothermic effect of melting to produce an asymmetric peak.

INTRODUCTION

Cinchocaine is a very strong-acting local anaesthetic, its application being restricted due to its high toxicity [1–3]. Methylsilyl derivatives of cinchocaine, which are characterized by different physicochemical properties from cinchocaine, are likely to exhibit greater affinity to the lipids and, owing to the increased molecular mass and size, they should stay longer at the site of administration [4]. This may result in a lower toxicity of the derivatives compared to the parent drug.

The methylsilyl derivatives of local anaesthetics with the Si–N bonds are compounds sensitive to moisture and consequently only their oily solutions are used in pharmacological investigations [4]. They must be sterilized over 20 min at a temperature of 393 K and an overpressure of 100 kPa. It is, therefore, important to determine the thermal stability of the methylsilyl derivatives of cinchocaine.

EXPERIMENTAL

Four silicon derivatives of the diethylaminoethyl amide of 2-butoxyquinoline-4-carboxylic acid (cinchocaine, nupercaine) of the general formula pre-

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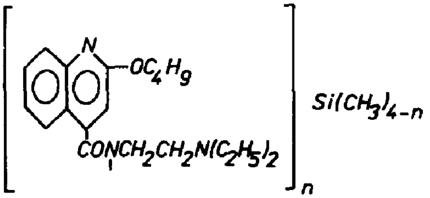

Fig. 1. General formula of silicon derivatives of diethylaminoethyl amide of 2-butoxyquinoline-4-carboxylic acid.

sented in Fig. 1 have been investigated. The methods of syntheses and the results of chemical analyses of the compounds have been described by Teodorczyk [5].

The DTA, TG and DTG curves of the thermal decomposition of the compounds examined were recorded using an OD-103 derivatograph model 3427–1500 ° C (MOM, Hungary). All measurements were made under identical conditions. The weighed 200-mg samples in a platinum crucible of 9.5 mm diameter were heated under an air atmosphere at a heating rate of 5 K min^{-1} up to a final temperature of 1073 K. α-Al_2O_3 was used as the reference.

RESULTS AND DISCUSSION

Thermal decomposition

The DTA, TG and DTG curves of the thermal decomposition of the compounds examined are presented in Fig. 2, whereas the temperature ranges and the mass losses corresponding to them for the successive decomposition stages are listed in Table 1.

From the analysis of the data obtained it follows that there exists a very great similarity in the decomposition of the methylsilyl derivatives of cinchocaine. Over the temperature range of 313–353 K endothermic effects associated with the melting of the compounds are observed on the DTA curves. The shape of the curves indicate that melting is not immediately followed by thermal decomposition. Only a mass loss of 0.5–1% is observed, associated with the slow evaporation of the molten compounds. This is confirmed by a wide and shallow endothermic effect on the DTA curve and by a slight deviation of the TG and DTG curves from the base line.

An abrupt mass loss associated with the beginning of the thermal decomposition of methylsilyl derivatives is not observed until the temperature range 443–468 K is reached. The value of the mass loss at this stage amounts to 82% for the trimethylsilyl derivative and gradually decreases to 79% for the tetrasubstituted silicon derivative. Also, the height of the DTG

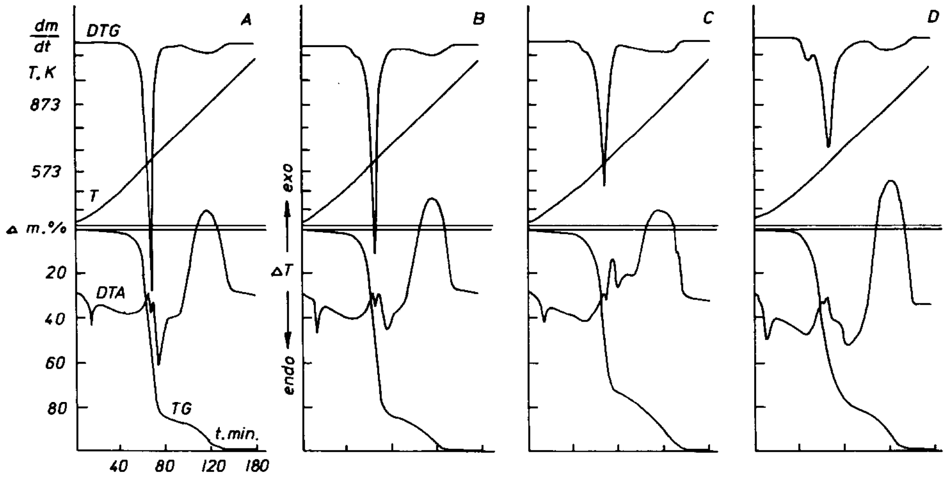

Fig. 2. DTA, TG and DTG curves of the thermal decomposition of: (A) trimethylsilyl derivative ($n = 1$), (B) dimethylsilyl derivative ($n = 2$), (C) methylsilyl derivative ($n = 3$) and (D) tetrasubstituted silicon derivative ($n = 4$) of cinchocaine.

peak decreases with a simultaneous widening at the base of the effect. The changes in the shapes of the TG and DTG curves show that the thermal decomposition rate of the methylsilyl derivatives of cinchocaine decreases with the increase of the number of cinchocaine radicals in the compound being decomposed.

The end of the second decomposition stage of the compounds examined is not distinctly pronounced on the TG and DTG curves since it overlaps the

TABLE 1

Results of the thermogravimetric analysis of silicon derivatives of cinchocaine (TR = temperature range (K), ML = mass loss (%))

Empirical formula	n [a]		Decomposition stages			
			I	II	II/III	III
$C_{23}H_{37}N_3O_2Si$	1	TR	333 [b]	443-673	673-763	763-963
		ML	0.5	82.0	4.0	13.5
$C_{42}H_{62}N_6O_4Si$	2	TR	343 [b]	458-693	693-768	768-958
		ML	1.0	81.0	3.5	14.5
$C_{61}H_{87}N_9O_6Si$	3	TR	348 [b]	458-678	678-768	768-953
		ML	1.0	74.5	6.0	18.5
$C_{80}H_{112}N_{12}O_8Si$	4	TR	348 [b]	468-723	723-773	773-953
		ML	1.0	79.0	3.0	17.0

[a] n = Number of cinchocaine radicals in the compound.
[b] $= T_{max}$ of the endothermic effects associated with the melting.

TABLE 2

Energy values and ionic character of some bonds present in silicon derivatives of cinchocaine

Bond	Energy values (kJ mol^{-1})			Ionic character (%) [6]
	[6]	[7]	[8]	
C–C	355			0
C–N	276	305		6
Si–C	313			11
Si–N	319	322		30
Si–O	374	451	422–494	51

beginning of the third stage. Owing to this, an intermediate stage II/III is specified in Table 1. It runs over a temperature range of 50–90 K with a small mass loss of only 3–6%. It is accompanied by a slight deviation of the DTG curve from the horizontal, indicating a very small almost constant, rate of mass loss.

The coked residue after the decomposition is burned in the third stage. This process is accompanied by a wide and shallow effect on the DTG curve and by an exothermic DTA effect. The surface area of this effect is proportional to the heat released during the burning and it gradually increases, reaching the maximum value for the tetrasubstituted silicon derivative. This is in agreement with the observations made in the second decomposition stage. The thermal decomposition of the methylsilyl derivatives of cinchocaine ends definitively at 953–963 K.

From the data contained in Table 2 it follows that the C–N bond is the least stable of all bonds in the molecules of the methylsilyl derivatives of cinchocaine. This bond can be assumed to be cleaved first in the molten compound. Along with the methylsilicon unit, the diethylaminoethyl radical is liberated, probably in the form of fragments also containing C–N bonds. On the other hand, the low energy value of the Si–N bond causes the volatile methylsilicon unit to be liberated from the system without forming silicon dioxide as a residue.

The probability of this type of decomposition is additionally confirmed on the DTG curve by the effect which has already appeared at about 523 K with the dimethylsilyl derivative. Its surface area increases with the increase of the number of cinchocaine radicals in the compound.

Differentiation of the DTA curve

The analysis of the shape of the endothermic DTA peaks was conducted by Stoch's method [9–11]. It consists in differentiating the DTA curves as a result of plotting the distance between the successive points as determined by the endothermic effect against the duration of the measurement at a given moment. To eliminate the dependence of the amplitudes of the

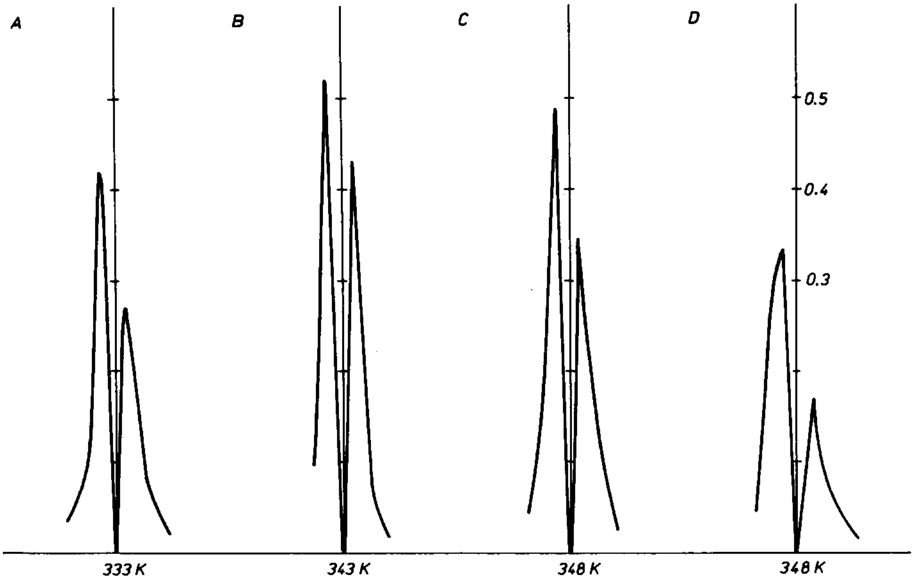

Fig. 3. Differential DTA curves of endothermic effects associated with the melting of: (A) trimethylsilyl derivative ($n = 1$), (B) dimethylsilyl derivative ($n = 2$), (C) methylsilyl derivative ($n = 3$) and (D) tetrasubstituted silicon derivative ($n = 4$) of cinchocaine.

differential DTA curve on the magnitude of the endothermic effect the following relative quantity was used:

$$\left| \frac{\mathrm{d}(\Delta T / \Delta T_{\mathrm{m}})}{\mathrm{d}t} \right| = \mathrm{f}(t) \tag{1}$$

where ΔT is the distance between the successive points as determined by the DTA curve, ΔT_{m} is the amplitude of the effect on the DTA curve and t is the duration of the measurement.

In Fig. 3 are presented the differential DTA curves of endothermic effects associated with the melting of the methylsilyl derivatives of cinchocaine. The left-hand part of the plot characterizes the rate of temperature increase on the DTA curve from the initial temperature of the effect to the temperature of the final point, whereas the right-hand part illustrates the rate of temperature increase over the range from the final point to the end of the thermal effect. This allows us to compare the course of the left- and right-hand sides of the DTA peak, as well as the DTA effects, with each other.

The height ratio of both maxima on the differential curve determines the shape factor of the DTA peak. It amounts to 1.53 for the trimethylsilyl derivative, 1.22 for the dimethylsilyl derivative, 1.43 for the methylsilyl derivative and 2.00 for the tetrasubstituted silicon derivative of cinchocaine.

The calculations conducted show the analysed peaks to be characterized by an asymmetric shape.

CONCLUSIONS

From the investigations it follows that the successive introduction of the cinchocaine radicals into the methylsilyl unit is reflected by the shape of the DTA, TG and DTG curves of the thermal decomposition of the methylsilyl derivatives of cinchocaine. It is particularly distinctly reflected by the temperatures of the final points of the endothermic DTA peaks associated with the melting of the compounds, as well as by the temperatures of the beginning of successive decomposition stages, which are shifted towards higher values with the increase of the molecular mass of the derivative being decomposed.

In the course of the decomposition of the trimethylsilyl, dimethylsilyl and methylsilyl derivatives of cinchocaine no formation of silicon dioxide has been found. This confirms the earlier investigations on the determination of the silica content in organosilicon compounds containing a methylsilicon unit [12].

The differentiation of the DTA curve has shown that the symmetrical-looking endothermic melting effect of the methylsilyl derivatives of cinchocaine has, in reality, an asymmetric shape. This is in agreement with the results of the investigations of Stoch [9], who observed endothermic effects of an asymmetric shape in the melting processes of certain inorganic compounds.

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