# Thermal degradation of basic alkoxy carbanilates in gas chromatograph

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Thermal degradation of two basic alkoxy carbanilates having local anaesthetic properties (pentacaine and heptacaine) was studied in the injector of a gas chromatograph. Decomposition of these compounds was found to proceed *via* cleavage of the labile carbamate bond yielding an alkoxyphenyl isocyanate and the corresponding amino alcohol. The thermal degradation products were identified by GC—MS analysis comparing their retention times and mass spectra with those of reference compounds.

Изучена термическая деградация двух основных алкоксизамещенных карбанилатов с анестезирующими свойствами (пентакаина и гептакаина) в инъекторе газового хроматографа. Разложение изучаемых соединений характеризуется расщеплением лабильной карбаматной связи, что ведет к образованию алкоксизамещенного фенилизоцианата и соответствующего аминоспирта. Продукты термической деградации были идентифицированы с помощью ГЖХ—масс-спектроскопического анализа посредством сравнения их времен удерживания и масс-спектров с параметрами синтезированных стандартов.

The investigation of basic alkoxy carbanilate type local anaesthetics revealed interesting pharmacological properties of pentacaine (*I*) and heptacaine (*II*) [1]. As part of this research, analytical studies have been conducted [2, 3].

The preliminary analytic information on pentacaine indicated [2] that it decomposes at temperatures above 160 °C in air to afford volatile products. The gas chromatographic separation of pentacaine on an OV-17 column showed two intense chromatographic peaks. Thermal decomposition of some alkyl *N*-phenyl carbamates has already been studied [4], phenyl isocyanates and the corresponding alcohols being the products of primary decomposition which can undergo further degradation.

This paper deals with the thermal degradation of pentacaine and heptacaine in the injector of a gas chromatograph.

## Experimental

Pentacaine (*I*, *trans*-2-(1-pyrrolidinio)cyclohexyl-3-pentyloxycarbanilate chloride), 3-pentyloxyphenyl isocyanate (*III*), and *trans*-2-(1-pyrrolidinyl)cyclohexanol (*IV*) were synthesized by *Beneš et al.* [5], heptacaine (*II*, 2-(1-piperidinio)ethyl-2-heptyloxycarbanilate chloride) and 2-heptyloxyphenyl isocyanate (*V*) were prepared by *Čižmárik et al.* [6], 2-(1-piperidinyl)ethanol (*VI*) was a commercial product of EGA-Chemie (Steinheim, FRG).

The GC—MS system consisted of a gas chromatograph JGC-20 K and mass spectrometer JMS-D 100 (Jeol, Japan). The carbamates were pyrolyzed in the injector of the gas chromatograph at 300 °C, concentrations of carbanilate bases being approximately 1 mmol $dm^{-3}$ in chloroform. Decomposition products were separated on a glass column (2 × 1000 mm), packed with 3 % OV-17 on Chromosorb W (Merck, Darmstadt, FRG), grain size 0.195—0.251 mm. The products were isothermally analyzed at 150 °C column temperature, 250 °C separator temperature, helium carrier gas (81 kPa), ionizing electron energy 23 eV, trap current 300 μA, and ionization chamber temperature 220 °C.

## Results and discussion

A simple chromatogram showing two intense chromatographic peaks (Fig. 1) resulted from thermal degradation of pentacaine. Mass spectra (Fig. 2) indentified the decomposition products as *trans*-2-(1-pyrrolidinyl)cyclohexanol (*IV*) and 3-pentyloxyphenyl isocyanate (*III*). To verify this assignment, retention times and mass spectra of degradation products were compared with those of reference substances synthesized. The elution of less volatile pyrolysis products, or of the unchanged compound was not observed even after rise of the column temperature to 270 °C. These results entitled us to suggest Scheme 1 for thermal degradation of pentacaine.

Thermal decomposition of heptacaine at analogous conditions is reflected by the chromatogram reproduced in Fig. 3. The identity of retention times and mass spectra (Fig. 4) with GC—MS data were the arguments for assignment of the structures of 2-(1-piperidinyl)ethanol (*VI*) and 2-heptyloxyphenyl isocyanate (*V*) to the degradation products analogously as with pentacaine. The GC—MS analysis of chloroform extracts of urine, plasma, and microsomal suspension after administration of pentacaine and heptacaine showed that thermal decomposition of these substances proceeded similarly regardless of their origin [7]. The same degradation products were obtained also with methanolic or ethereal solutions of the compounds under study.

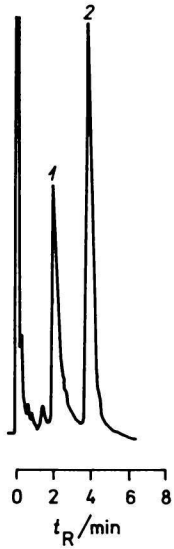



*Fig. 1.* Gas chromatogram of pyrolysis products of pentacaine.
*trans*-2-(1-Pyrrolidinyl)cyclohexanol (*IV*) (*1*); 3-pentyloxyphenyl isocyanate (*III*) (*2*).

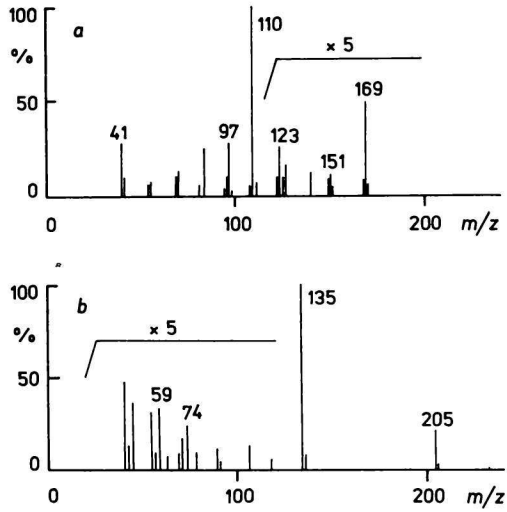
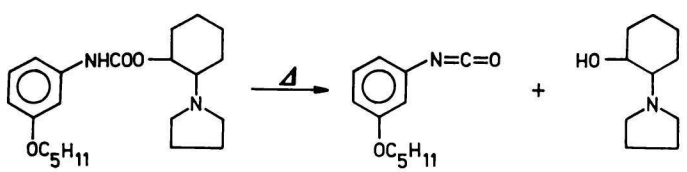



*Fig. 2.* Mass spectra (23 eV) of pyrolysis products of pentacaine (*cf.* chromatogram in Fig. 1).
Chromatographic peak of *trans*-2-(1-pyrrolidinyl)cyclohexanol (*IV*) (*a*); chromatographic peak of 3-pentyloxyphenyl isocyanate (*III*) (*b*).




*Scheme 1*

Thermal degradation of pentacaine

The defined and simple course of thermal degradation of pentacaine and heptacaine in the gas-chromatograph injector offers a possibility to monitor the drugs and their metabolites in biological samples by GC or GC—MS detection of their characteristic decomposition products.


*Fig. 3.* Gas chromatogram of pyrolysis products of heptacaine.
2-(1-Piperidinyl)ethanol (*VI*) (*1*); 2-heptyloxyphenyl isocyanate (*V*) (*2*).

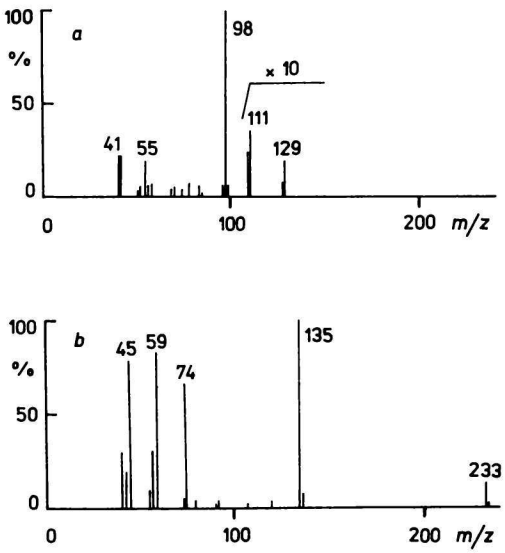



*Fig. 4.* Mass spectra (23 eV) of pyrolysis products of heptacaine (*cf.* chromatogram in Fig. 3).
Chromatographic peak of 2-(1-piperidinyl)-ethanol (*VI*) (*a*); chromatographic peak of 2-heptyloxyphenyl isocyanate (*V*) (*b*).

The use of gas chromatography in quantitative analysis of pentacaine and heptacaine shall be, however, limited to suitable thermally stable derivatives.

## References

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