DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 6(1), 99-104 (1980)

DETERMINATION OF THE HYDROLYSIS OF QUINOLINIUM-1-METHYLIODIDE-6-CARBOXY-METHYL ESTER BY GLC

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SUMMARY

A GLC method for the determination of the hydrolysis of quiolinium-1-methyliodide-6-carboxy-methylester is described. GLC is performed on porous polymer composed of ethylvinylbenzene cross-linked with divinyl-benzen (Polapak-Q). The retention times of methyl alcohol and the internal standare (tertiary butanol) are 2.8 and 6.3 min., respectively. The apparent pseudo-first order rate constants as a function of temperature (37°C and 50°C) in the presence of 6N HCl were calculated and found to be 2.6×10^{-2} min^{-1} and 2.7×10^{-2} min^{-1} respectively.

INTRODUCTION

This investigation was undertaken to study the hydrolysis of quinolinium-1-methyliodide-6-carboxy methyl ester (1) a new potential antimicrobial and antimalarial compound (Scheme I).

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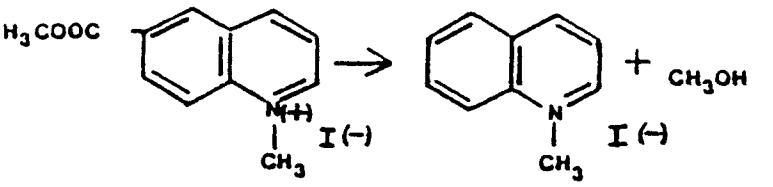

Scheme I

The classical analytical procedures could not be used for lack of specificity an/or accuracy e.g., UV spectroscopy was eliminated because preliminary studies showed an overlapping of the absorbance spectra of the hydrolytic product (quinolinium-1-methyliodide-6-carboxylic acid (II) with the parent compound (I).

Gas chromatography which is the method of choice in drug analysis since the second half of the sixties as reviewed by Gudzinowicz offers a solution to such problems. Therefore, it was decided to study the rate of hydrolysis of (I) by measuring the quantity of methyl alcohol produced during the reaction. This was done by utilizing a previously described GLC method by Machata, appropriately modified.

MATERIALS AND METHODS

Materials - The following were used: 6N HCl and tertiary Butanol[1], both of chromatographic grade.

Instrumentation - A gas chromatograph[2] equipped with a dual flame-ionization detector (F.I.D.) was used. The column was a coiled stainless steel 210 cm. x 3 mm. i.d., packed with Poln-pack Q (150-200 mesh)[3]. The column was preconditioned at 230°C for 18 to 20 hours prior to use. The helium flow rate was 60 mls/min., the hydrogen flow was 45 mls/min., and the air flow was 200 mls/min. The temperature of both the injection port and the F.I.D. was set up at 190°C. During the analysis, the column temperature was maintained at 160°C.

1 Fisher Scientific Co., 52 Fadem Rd., Springfield, NJ 07081
2 Hewlett-Packard 7620A, Packard Instrument Co., Downers Grove, Ill.
3 Waters Associates, Inc., Milford, MA 01757

PROCEDURE

One hundred fifty milligrams of (I) was dissolved in 25 mls. of distilled water. To this 25 mls. of 6N HCl was added, with continuous stirring, and immediately after the addition of the acid 1 ml. of the solution was transferred to a 2 mls. capacity mini-injection vial. To this 5.0 ul. of the internal standard (tertiary butanol) was added. From this 5.0 ul was directly injected into the gas chromatogram for the determination of liberated methyl alcohol Samples from the reaction system were injected at: 5, 10, 15, 25, 35, 45, 55, 65 min. and 24 hour intervals. All samples were assayed in triplicate.

Following chromatography, a baseline was drawn and peak heights of methyl alcohol and internal standard were measured. The ratio of methyl alcohol and internal standard peak heights were calculated and the concentration of methyl alcohol was obtained by reference to the standard curve.

A standard curve was obrained by analysis of samples containing known quantities of methyl alcohol and internal standard. After plotting the peak height ratios of methyl alcohol to internal standard versus concentration of methyl alcohol, the best-fit straight line passing through the origin was drawn. A linear relationship was found to exist at least up to 26 ug/ml.

RESULTS AND DISCUSSION

The typical response of the internal standard and methanol to the chromatographic system is shown in Fig. 1. Methanol and the internal standard were adequately separated under the experimental conditions with retention time of 2.8 and 6.3 min. respectively. The column packing was Pora-pack-Q material which is a porous polymer composed of ethylvinyl-benzene cross-lined with divinylbenzene to form a uniform structure of a distinct pore size. The porous polymer beads serve the function of bothe the liquid phase and the solid support. The retention data is very constant since the pora-pack columns usually have no liquid phase to be lost by continual bleeding.

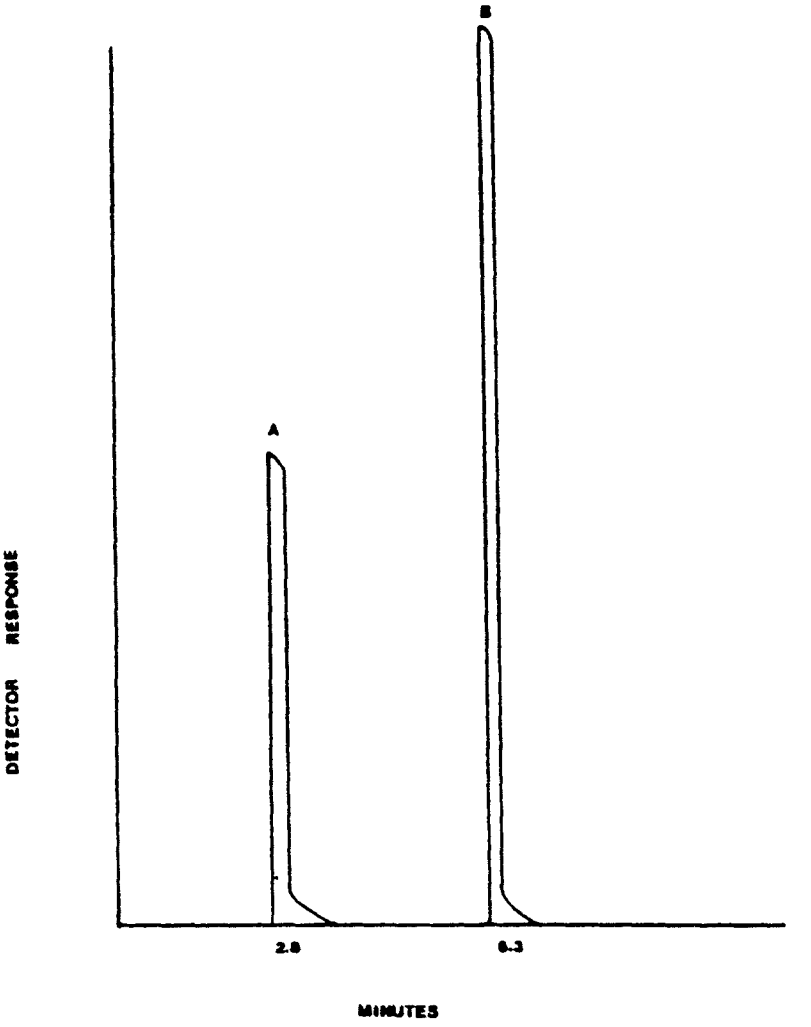

Figure 1. Typical chromatogram of (A) methanol (1 ug/liter) and (B) internal standard (5 ug/liters)

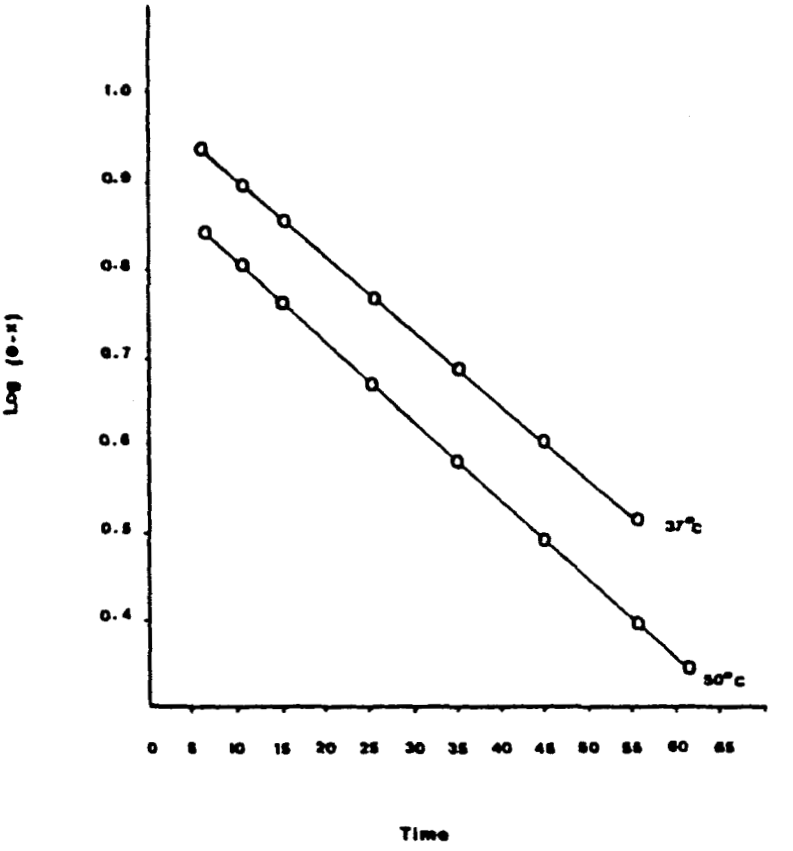

Figure 2. Apparent psewdo-first order rate constants as a function of temperature (37°C and 50°C) in the presence of 6N HCl

The apparent psuedo-first order rate constants as a function of temperature (37 C and 50 C) in the presence of 6N HCl are shown as Fig. 1 and are 2.6 x 10^{-2} min^{-1} and 3.7 x 10^{-2} min^{-1} respectively as were calculated from the slope of the lines. At room temperature the reaction rate was too slow for any appreciable amount of methyl alcohol

to be detected. The total quantity of methyl alcohol liberated at the end of the experiment (24 hours) was taken as the initial concentration and it was used as such in calculations of the pseudo-first order rate constants. The reaction is taken as a pseudo-molecular one since the concentration of water used is negligible with respect to the ester (I).

REFERENCES

1. B.J. Gudzinowicz, "Gas Chromatography Analysis of Drugs and Pesticides" Dekker, N.Y. (1976).
2. G. Machata, "Determination of Alcohol in Blood by Gas Chromatographic Head Space Analysis", Clinical Chem. Newsletter, 4 (2), 29, 1971.
3. H.M. Mittair and E.J. Bonelli, "Basic Gas Chromatography", Varian Aerograph, Walnut Creek, California 94598 (1969).