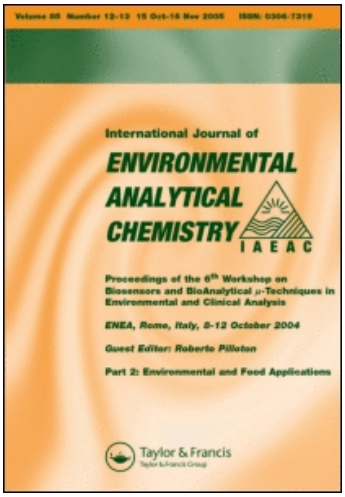

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Triclocarban and Cloflucarban: I. Gas-Liquid Chromatography of Triclocarban, Cloflucarban and Related Anilines after Silylation

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Triclocarban and Cloflucarban: I. Gas-Liquid Chromatography of Triclocarban, Cloflucarban and Related Anilines after Silylation

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A method is presented for the simultaneous determination of Triclocarban (N-(4-chlorophenyl)-N′-(3,4-dichlorophenyl)urea, [101-20-2] Cloflucarban (N-(4-chlorophenyl)-N′-[4-chloro-3-(trifluoromethyl)phenyl]urea, [369-77-7]) and the related anilines, 4-chloroaniline, 3,4-dichloroaniline and 4-chloro-3-trifluoromethyl aniline.* Temperature programmed gas chromatography, after preparing trimethylsilyl derivatives is employed, using MSTFA (N-methyl-N-trimethyl-silyl trifluoroacetamide) as the derivatizing agent and a column with Dexsil 400 as the stationary phase. On a glass column quantitative results are obtained and linear calibration plots are obtained using phenanthrene as an internal standard, for 20-400 ng Triclocarban with a flame-ionization detector. Well-resolved gas chromatograms are obtained for the several compounds.

*KEY WORDS: Triclocarban, Cloflucarban, antimicrobial agents, gas chromatography.

INTRODUCTION

Triclocarban, (N-4(-chlorophenyl)-N′-(3,4,-dichlorophenyl)- urea [101-20-2]), and Cloflucarban, (N-(4-chlorophenyl)-N′-[4-chloro-3-(trifluoromethyl)-phenyl]-urea [369–77–7]), are antimicrobial agents in common use in medicated "deodorant" soap and healthcare personnel hand-wash, either singly or in combination. The use of the antimicrobial agents

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(AMA's) in soap bars in the U.S. is in excess of 100,000 kg per year.[1] In the case of Triclocarban (TCC) and Cloflucarban (CFC) little is known concerning their fate once they reach the environment, and there is need for developing analytical methods capable of detecting these substances and their degradation products at the very low levels at which they may be present in the environment.

The usual methods of determination of urea derivatives involve acidic or basic hydrolysis to the corresponding amines, followed by gas chromatographic determination, either directly or after derivatization. However, since the AMA's are expected to yield anilines as degradation products, methods based on such hydrolysis will not be suitable for detecting the AMA's in the presence of their degradation products. Direct GLC measurements are not possible because of the low volatility of the AMA's, but suitable derivatives can be prepared and measured.

Recently König[2] described conditions for the gas chromatography of antimicrobial agents using a silicone-rubber W982 on the support as stationary phase after silylation with a hexamethyldisilizane-trimethylchlorosilane-pyridine mixture, using flame ionization detection. TCC and CFC appeared together in the temperature-programmed run. Further, the sensitivity was quite low. Subsequent efforts to separate TCC and CFC have been unsuccessful: Wilson[3] was unable to separate TCC and CFC by TLC; Sheppard and Wilson[4] reported that TCC and CFC were eluted in the same fraction using partition chromatography; Demerst and Yates[5] were likewise unsuccessful in separating TCC and CFC using high-pressure liquid chromatography and gas liquid chromatography.

A method is now presented for the simultaneous GLC determination of TCC, CFC, and the related anilines: 4-chloroaniline [106-47-8], 3,4-dichloroaniline[95-76-1] and 4-chloro-3-(trifluoromethyl)aniline [320-51-4]. The procedure involves derivatization with N-methyl-N-trimethylsilyltrifluoroacetamide, (MSTFA), followed by GLC separation on a Dexsil 400 stationary phase. The method is sensitive to nanogram levels for the AMAs.

EXPERIMENTAL

Gas chromatography

GLC determinations were made using a Varian Aerograph 1520-c Series GC equipped with a flame ionization detector, on a 4′ × 1/8″ o.d. Nickel column containing 10% Dexsil 400 on 100-120 mesh Chromosorb WHP, or a 5′ × 1/4″ o.d. glass column containing 3% Dexsil 400 on 100-120 mesh Supelcoport AW-DMGS (Supelco, Inc., Bellefonte, PA).

The new column was conditioned overnight at 270°C and then deactivated with several 5 μl injections at 150°C of Silyl-8 column conditioner. (Pierce Chem. Co., Rockford, IL), determinations were made at 210°C isothermal column temperature, or with temperature programming between 128°C and 248°C at 6° per minute. The injection port and the detector were maintained at 210° and 275°C respectively.

Isothermal runs were made at 210°C. Carrier gas: Nitrogen at 25 ml per minute. Electrometer sensitivity: 8×10^{-12} amperes per mV.

Temperature Programmed runs: At 6°C per minute between the temperature limits specified. Sensitivities varied between 1×10^{-11} and 8×10^{-10} amperes per mV.

For the calibration curves the ratio of areas under the peak multiplied by the amplification factor of the target substance and of the internal standard were calculated. In the case of the TCC calibration (Figure 5) the areas of peaks for less than 50 ng were too small to be measured by the Integrator. Graphical tringulation methods were used to measure the peak areas after calculating the ratio between measured area and integrator units by measuring and integrating more than 20 peaks.

Data for TCC calibration curve (glass column) were obtained using a Varian 1400 Model GC with flame ionization on a 2 m × 2 mm i.d. (1/4" o.d.) glass column containing 3% Dexsil 400 on 100-120 mesh Chromosorb WHP. (Chrompack, Berlin, Germany). The temperature programmed separations were conducted between 210° and 270°C at 6° per minute. (Figure 5).

Reagents

The following were used: Triclocarban (Pfalz & Bauer Co.), Cloflucarban (Ciba-Geigy Co. "High Purity"), ethanol (USP grade), N-methyl-N-trimethylsilyltrifluoroacetamide (MSTFA) (silylation grade) (Pierce Chem. Co.); other materials were reagent grade. The following were employed as degradation standards of the AMA's: 4-chloroaniline, 3,4-dichloroaniline, 4-chloro-3-trifluoromethylaniline.

Sample preparation

50 μl of a solution of the AMA or a mixture of the AMA's and degradation standards are transfered to a 300 μl Reacti-vial equipped with a Teflon Mininert valve closure (Pierce Chem. Co.) by means of a syringe. The solvent is evaporated from the open vial to just dryness using a gentle stream of dry nitrogen. The closure is placed on the vial and 50 μl of MSTFA are injected (excess MSTFA is required to act as solvent). The Mininert valve is closed and the vial incubated in the oven at 90°C for 90 minutes, or 15 minutes when only the AMA's are involved. After cooling to room temperature, phenanthrene

internal standard is added by injecting into the silylated solution 0.5 μl of a solution containing 10 μg/μl phenanthrene in methylene chloride. The sample is mixed thoroughly and 1 or 2 μl are drawn for injection into the GC.

RESULTS AND DISCUSSION

GLC DETECTION limits

Minimum detectable levels (MDL's) for the AMA's were determined for both metal and glass columns. Standard curves were obtained by plotting the ratio of the sample signal peak area to internal standard signal peak area against the mass of AMA injected.

TCC could be detected down to 0.4 ng when determined by isothermal GC on the nickel column (Figure 1 and 2), while TCC and CFC could be detected down to only 96 and 78 ng, respectively, on the same column using temperature programmed GLC (Figure 3).

The non-linear standard curves and the reduced response under temperature programmed conditions with the nickel column are attributed to on-column thermal decomposition of the bis-(trimethylsilyl) derivatives to the mono-(trimethylsilyl) compound. This decomposition has been confirmed by Hoar and Bowen[6] in the case of TCC by mass spectra of the bis-(trimethylsilyl) derivative eluted from the column. In GC chromatograms the decomposition causes double peaks. The smaller second peak, believed to be due to the mono-silylated derivative, increases at the expense of the main peak when derivatized samples are allowed to stand several days before analysis.

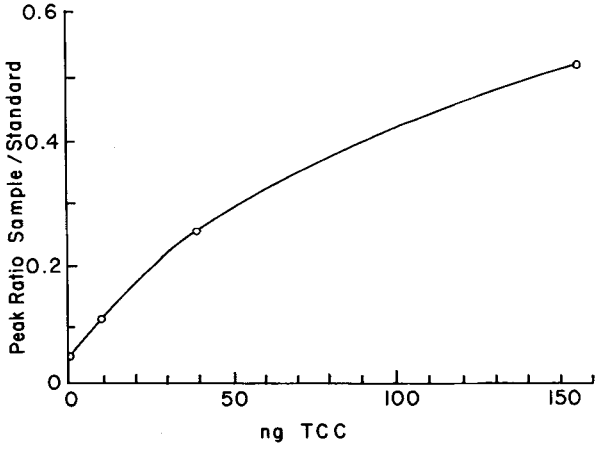

FIGURE 1 TCC calibration curve: Ratio of peak area of Triclocarban to peak area of Phenanthrene internal standard. Nickel column, 4' × 1/8", 10% Dexsil 400 on 100–120 mesh Chromosorb WHP. Isothermal at 210°C. FID detector at 8×10^{-12} A/mV. Recorder: 1 MV range.

FIGURE 2 Chromatogram of 0.78 ng TCC. Nickel column, conditions as in Figure 1.

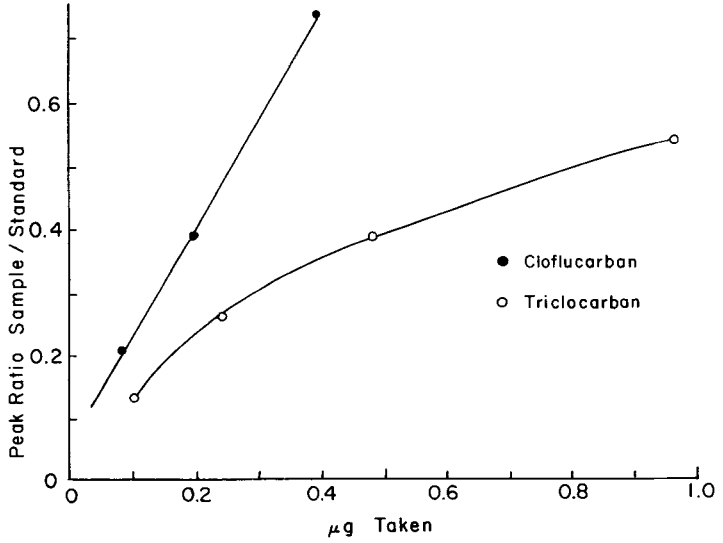

FIGURE 3 TCC and CFC calibration curves. Nickel column, conditions as in Figure 1, except temperature-programmed: 128°C to 248°C at 6° per minute.

The use of the glass column leads to excellent response for all the substances investigated. Figure 4 shows a tracing of a typical chromatogram obtained when a mixture containing TCC, CFC, 4-chloroaniline, 3,4-dichloroaniline and 4-chloro-3-(trifluoromethyl)aniline is derivatized and subjected to temperature programmed GLC separation between 128° and 248°C at 6° per minute. The peaks corresponding to TCC and CFC show some tailing as a result of the on-column decomposition of the bis-(trimethylsilyl) derivatives described above. In spite of this decomposition, TCC has been determined down to 17 ng with an overall standard deviation of 15%, the range of replicate results is within 5% for all but the lowest values (Figure 5). The response is linear to low nanogram levels.

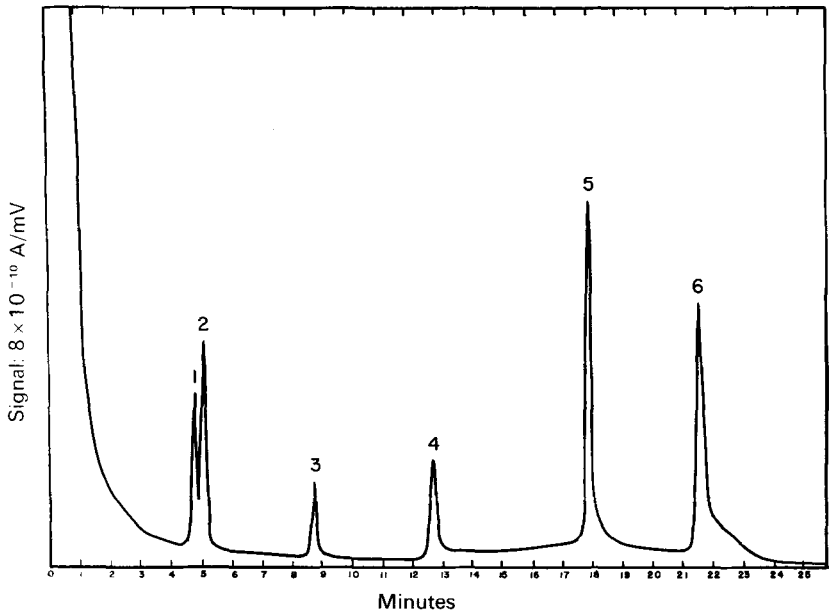

FIGURE 4 Chromatogram of a solution containing: (1) 4-chloro-3-(trifluoromethyl) aniline, 0.126 μg/μl; (2) 4-chloroaniline, 0.190 μg/μl; (3) 3,4-dichloroaniline, 0.095 μg/μl; (4) phenanthrene (internal standard), 0.111 μg/μl; (5) Cloflucarban, 1.66 μg/μl; (6) Triclocarban, 1.80 μg/μl. 1 μl injected. Glass column, 5′ × 2 mm i.d., 3% Dexsil 400 on 100–120 mesh Supelcoport. Temperature programmed at 128°C at 6° per minute. FID detector at 8×10^{-10} A/mV.

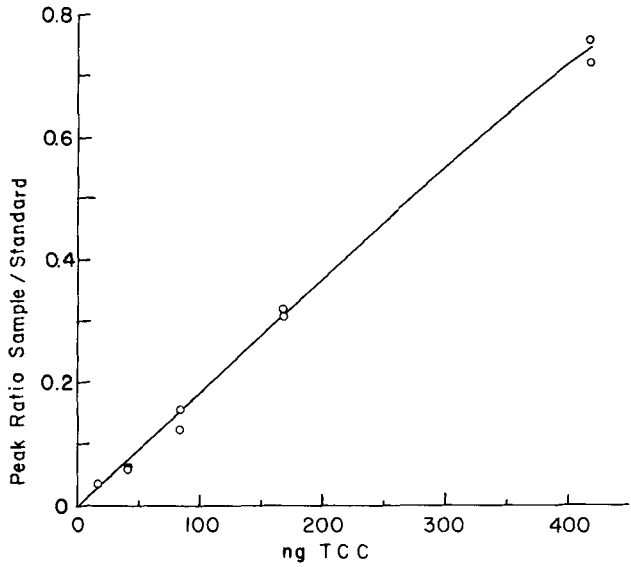

FIGURE 5 TCC calibration curve: Ratio of peak area of Triclocarban to peak area of internal standard (phenanthrene). Glass column, 2 m × 2 mm i.d., 3% Dexsil 400 on 100–120 mesh Chromosorb WHP. Temperature-programmed: 210°C–270°C at 6° per minute. FID detector at 1 to 16×10^{-11} A/mV.

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