A novel method for the identification of alcohols in complex mixtures

The successful analysis of alcohols in complex mixtures depends upon finding a suitable method for either extracting the alcohols or detecting them in the presence of other compounds.

In these laboratories, two published methods have been used in our studies on tobacco smoke condensate[1,2]. Both depend upon the conversion of the alcohols to derivatives, followed by isolation by extraction or column chromatography. The results obtained by these methods showed a measure of agreement, and support the results of other workers[3,4]. Both methods have the disadvantage of being lengthy and complicated. A new method was therefore sought which would be simple and rapid, and which would avoid as far as possible the prolonged action of heat and reagent on labile compounds.

A halogen-sensitive gas–liquid chromatography (GLC) detector was already in use in this department when the problem arose and the possibility of producing halogenated derivatives of alcohols and utilising the detector to examine them in the presence of other compounds seemed a worthwhile approach. The reaction of alcohols with chloroacetyl chloride to form halogenated esters was investigated

Materials and method

The work was carried out on a modified Pye Argon Chromatograph oven using an A.E.I. Ozotron type J halogen-sensitive detector[5].

The argon detector and aluminium heater bars were removed from the Pye oven to enable it to take a U-shaped $^1/_4$ in. glass column, and the oven top modified to take the injection system and detector shown in Fig. 1.

This detector has been investigated by other workers[6] and its performance, linearity and limits of detection determined. For this work it was found that high sensitivity was not required, and a heater supply of 4.6 V a.c. at 6.7 A and H.T. of 108 V d.c. was adequate for a 2 to 20 μg loading of the halogenated esters. Nitrogen was used as both carrier and dilution gas, the flows being maintained at 40 ml·min^{-1} and 110 ml·min^{-1}, respectively. Injection was on column with no flash heaters.

All I.R. spectra were scanned on a Hilger and Watts H. 800 spectrophotometer, the samples being prepared as capillary films.

Preparation of alkyl chloroacetates

All the chloroacetates used could have been prepared by addition of chloroacetyl chloride to a solution of the alcohol in benzene at room temperature, but when dealing with complex mixtures the reaction mixture was actually refluxed. The method adopted for the preparation of all chloroacetates was as follows. The alcohol (1 g), or mixture was dissolved in benzene (10 ml, A.R.), the required amount of chloroacetyl chloride (at least twice the molar equivalent) was added dropwise, and the mixture boiled under reflux for one hour. After allowing the mixture to cool to room temperature a large excess (5 ml) of ethanol was added, and the mixture allowed to stand for a further 30 min. The mixture was made up to 50 ml with benzene and was then ready for chromatographic examination.

When this method was used with complex mixtures it was found necessary to determine the optimum amount of chloroacetyl chloride needed, since the presence

of a large excess of unreacted chloride at the end of the reaction leads to a very large ethyl chloroacetate peak, possibly inhibiting the detection of smaller peaks in the same region.

In early experiments the excess of chloroacetyl chloride was decomposed by washing the mixture with sodium bicarbonate. This was satisfactory, but the presence of alkali tended to hydrolyse some of the more reactive chloroacetates.

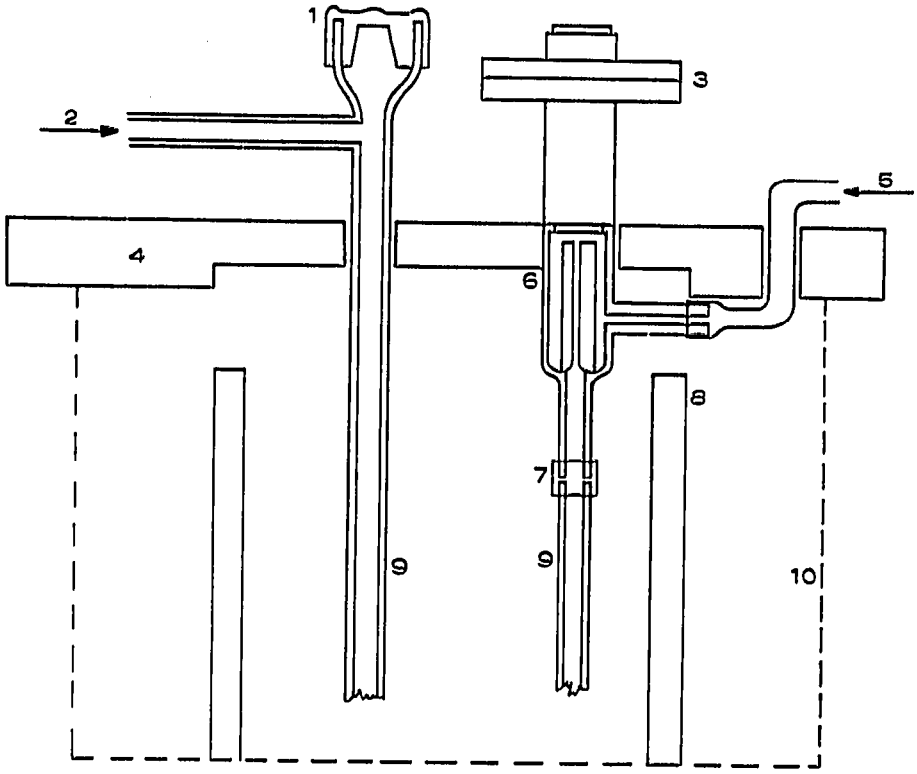

Fig. 1. Modified Pye argon chromatograph oven. 1 = Rubber serum cap; 2 = carrier flow; 3 = detector; 4 = oven top; 5 = detector flow; 6 = Pyrex adaptor; 7 = silicone rubber; 8 = aluminium heater tube; 9 = 2.2 m $^1/_4$ in. column; 10 = heating jacket.

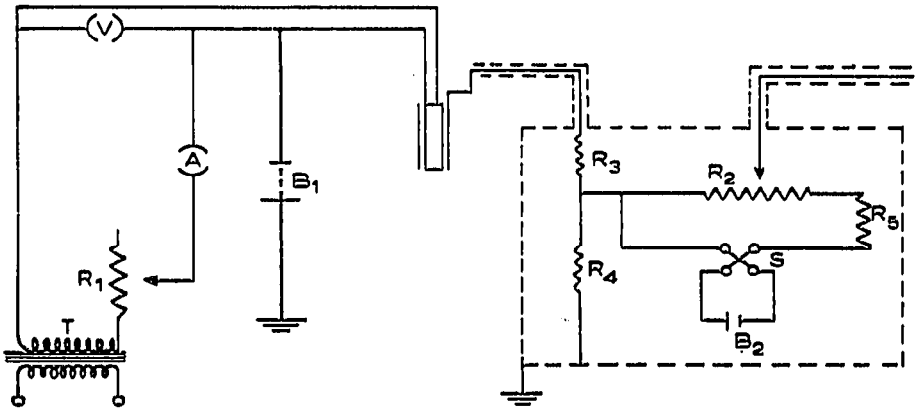

Fig. 2. Circuit used for the halogen-sensitive detector. R_1 = 1 Ω 10 A variable resistance; R_2 = 250 Ω 10 turn variable resistance; R_3 = 1 MΩ; R_4 = 1.5 kΩ; R_5 = 12 kΩ; S = backing-off polarity switch; T = 240/6 V constant voltage transformer; B_1 = 108 V H.T. battery; B_2 = 9 V backing-off battery; V = 0–10 V a.c. voltmeter; A = 0–10 A a.c. ammeter.

It is probable that phenols would react in a similar manner to alcohols, so that it might be necessary to remove these, and also amines, from a mixture prior to reaction with chloroacetyl chloride.

Results

Chloroacetates of most of the primary alcohols and many of the secondary and tertiary alcohols were prepared up to tridecanol. Chloroacetates were also prepared from several unsaturated alcohols, cyclopentanol, cyclohexanol, citronellol, menthol, tetrahydrofurfuryl, benzyl and β-phenylethyl alcohols. A chromatogram of some of these esters obtained at 200° is shown in Fig. 3. Attempts to produce a chloroacetate from furfuryl alcohol failed owing to the rapid polymerisation of the alcohol under acid conditions.

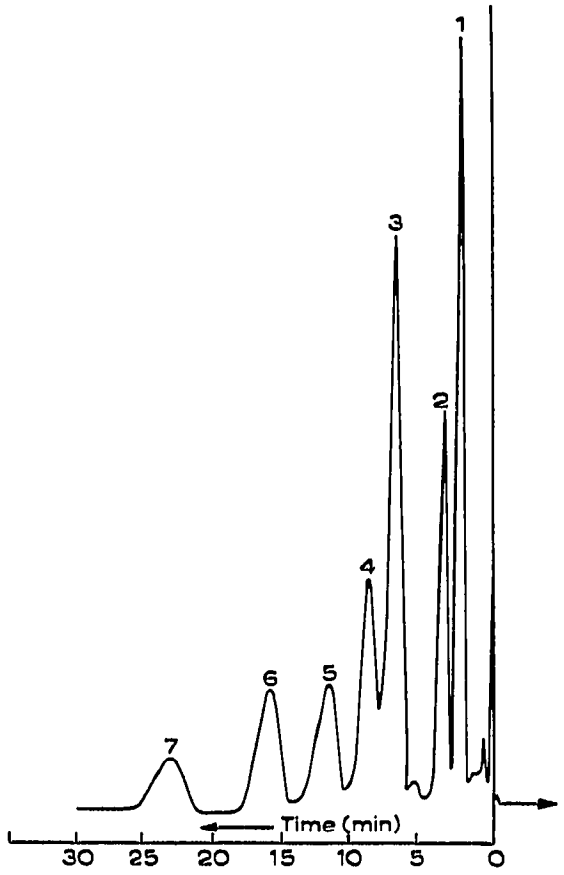

Fig. 3. Synthetic mixture run on 2.2 m 5% Reoplex 400 on 100/120 mesh Celite at 200°. 1 = Cyclopentyl chloroacetate; 2 = cyclohexyl chloroacetate; 3 = menthyl chloroacetate; 4 = tetrahydrofurfuryl chloroacetate; 5 = *n*-decyl chloroacetate; 6 = benzyl chloroacetate; 7 = β-phenylethyl chloroacetate.

All chloroacetates which were prepared were examined by I.R. spectroscopy. The spectrum of the ethyl chloroacetate was found to be identical with the spectrum of authentic ethyl chloroacetate purchased from B.D.H.*. This was the only chloroacetate commercially available, but the spectra of the other chloroacetates showed the type of absorption expected from α-halogeno esters.

* British Drug Houses Ltd., Poole, Dorset, Great Britain.

In the concentrated form many of the esters decomposed, but in dilute benzene solution they could be kept for several weeks.

A number of non-alcoholic neutral compounds were subjected to the reaction to determine whether any interference would be expected from such compounds if they were present in alcohol-containing mixtures.

Twenty-four compounds were investigated: acetaldehyde; acetone; acetophenone; amyl acetate; anisole; benzaldehyde; benzene; benzyl acetate; *n*-butyraldehyde; camphene; citral; cyclohexanone; cyclopentanone; dimethyl acetal; ethyl acetate; furfuraldehyde; hexaldehyde; isopropyl acetate; limonene; linalyl acetate; mesityl oxide; methyl amyl ketone; methyl benzyl ketone; 2-nonanone.

Of these cyclohexanone, hexaldehyde and butyraldehyde gave very small amounts of halogenated product possibly due to impurities, and acetaldehyde gave rather more interference than expected. The peaks obtained from the acetaldehyde reaction were eluted very early and did not appear from their retention times to be halogen esters.

As an example of the results obtained by this method, Fig. 4 shows a chromatogram of alcohol chloroacetates derived from tobacco smoke neutral condensate, *i.e.*, a condensate from which acids, bases and phenols have been extracted.

The method has not been extended beyond the tridecanol region owing to the

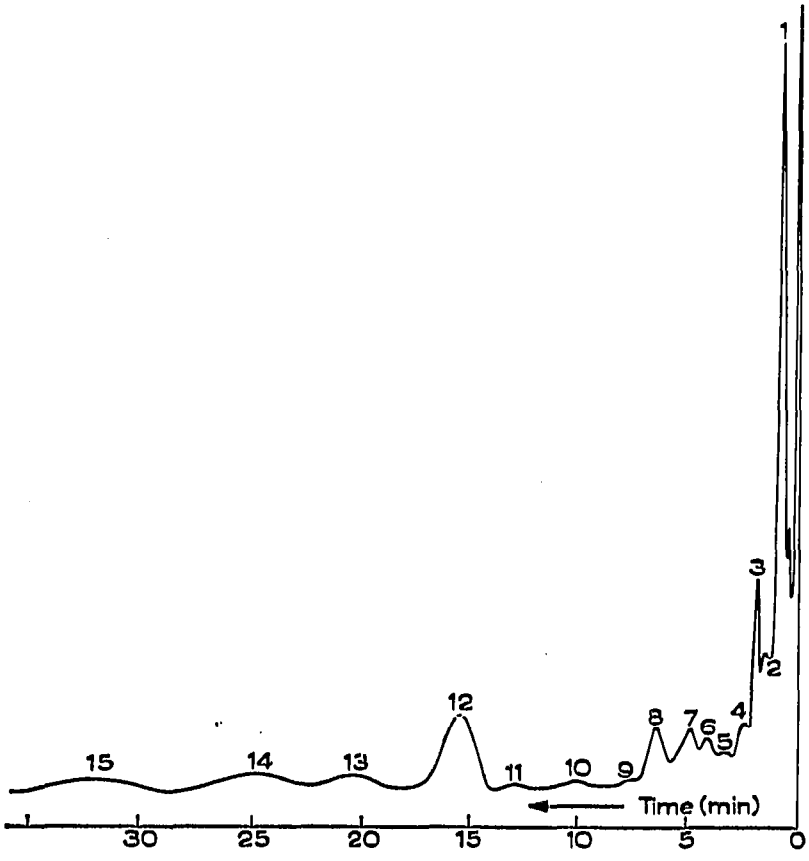

Fig. 4. Neutral smoke condensate sample on 2.2 m 5% Reoplex 400 on 100/120 mesh Celite at 200°. 1 = Isopropyl chloroacetate; 5 = isohexyl chloroacetate; 7 = *n*-hexyl chloroacetate; 10 = isooctyl chloroacetate; 11 = *n*-octyl chloroacetate; 14 = *n*-decyl chloroacetate; 15 = isoundecyl chloroacetate.

temperature limitations of the Pye argon chromatograph oven, but there appears to be no reason why this method should not be applicable to the higher molecular weight alcohols.

Conclusion

Reaction of neutral, alcohol-containing mixtures with chloroacetyl chloride, and analysis of the products by a gas–liquid chromatograph incorporating a halogen-sensitive detector, has been shown to offer a useful method for the identification of alcohols in such mixtures. The method is quick, and very sensitive. Satisfactory results were obtained with most of the alcohols studied, and interference from non-alcoholic compounds is negligible.

This method should also be applicable to the analysis of phenols, and the use of GLC with a halogen-sensitive detector may well have great potential value in the examination of other types of compound in complex mixtures if suitable halogenated derivatives can be prepared.

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