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Note

Detection of alcohols at the femtogram level as pentafluorophenyldimethylsilyl ethers

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In an investigation of fluorocarbon containing dimethylsilyl ethers suitable for the gas chromatography (GC) of sterols with electron capture detection (ECD), we discovered the usefulness of pentafluorophenyldimethylsilyl ethers (contracted to flophemesyl for convenience)¹. The most useful reagents for converting sterol hydroxyl groups to flophemesyl ethers were flophemesylamine, flophemesyldiethylamine and flophemesyl chloride^{2,3}. Flophemesylamine was found to be a selective reagent, reacting only with unhindered primary and secondary hydroxyl groups and not at all with unprotected ketone groups. As well as establishing the conditions for the formation of flophemesyl ethers of a wide range of sterol hydroxyl groups, it was also shown that these derivatives had good GC properties and were excellent derivatives for mass spectrometry (MS) as the flophemesyl group influenced the nature of the fragmentation pathway giving useful and intense diagnostic ions with a greater percentage of the ion current carried by carbon fragments when compared with the trimethylsilyl ethers⁴.

In connection with our work on volatile chemicals in insects a reagent was required which permitted the separation, characterization and determination of volatile alcohols. In this note we wish to describe the evaluation of flophemesyl ethers for this purpose.

EXPERIMENTAL

Flophemesylamine and flophemesyl chloride were obtained from Lancaster Synthesis (St. Leonard Gate, Lancaster, Great Britain). The flophemesyl ethers of primary or secondary alcohols in pyridine were formed quantitatively and instantaneously by addition of equal volumes of the above reagents. Tertiary alcohols (*e.g.*, 2-methylpropan-2-ol) required approximately 10 min at 25 °C for complete reaction.

GC was performed on both a Pye Series 104 gas chromatograph with flame ionization and a pulsed ⁶³Ni electron capture detector and a Pye Unicam GCV with flame ionization and constant-current ⁶³Ni electron capture detectors. The pulsed

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detector was operated with a pulse space of 50 μsec , pulse width 0.75 μsec and height 47–60 V with a detector oven temperature of 300 °C. The constant-current detector was operated with a detector current of 10 nA and a detector oven temperature of 350 °C.

Combined GC–MS was performed with a Pye Series 104 chromatograph coupled through a Watson-Bieman separator maintained at 300 °C with a helium flow-rate of 18 ml/min to an Hitachi-Perkin Elmer RMU-6 mass spectrometer operated with a trap current 60 μA , electron energy 80 eV and accelerating voltage 1.8 kV.

RESULTS AND DISCUSSION

A difficulty in determining volatile substances such as low molecular weight alcohols is to ensure that sufficient separation from the solvent front and from other compounds of similar carbon number can be achieved. This is the more difficult if detection at trace levels is also required. The flophemesyl ethers produce volatile derivatives of good peak shape which are well resolved from interfering substances in the solvent front and are also well separated from each other (Table I). The large

TABLE I

RETENTION TIME DATA FOR LOW-MOLECULAR-WEIGHT ALCOHOLS AS THEIR FLOPHEMESYL ETHERS

Column (5 ft.), 3% OV-101 on Suprasorb AW HMDS; nitrogen flow-rate, 50 ml/min.

Alcohol	Retention time (min)		
	Column temperature (°C)		
	120	170	230
Methanol	2.3		
Ethanol	2.9		
Propan-1-ol	4.8		
Propan-2-ol	3.4		
Butan-1-ol	7.0		
Butan-2-ol	5.5		
2-Methylpropan-2-ol	4.4		
Pentan-2-ol	8.2		
Pentan-3-ol	8.7		
Cyclopentanol	13.9		
Hexan-1-ol	—	3.4	
Hexan-2-ol	—	2.7	
Hexan-3-ol	—	2.5	
Cyclohexanol	—	4.0	
2-Ethylhexan-1-ol	—	5.1	
Benzyl alcohol	—	6.3	
Octan-1-ol	—	7.2	
Octan-2-ol	—	5.2	
Cyclo-octanol	—	9.9	
Dodecan-1-ol	—	—	3.6
Cyclododecanol	—	—	4.4
Butan-2,3-diol	—	—	3.0
Triethylene glycol	—	—	5.8

additional molecular weight increment obtained by the formation of flophemesyl ethers should be particularly useful in separating alcohols containing different numbers of hydroxyl groups. Also those components of a mixture with similar carbon numbers which do not form derivatives will not interfere as the alcohol is selectively moved to a position of longer retention time, which both aids resolution and provides useful information about the nature of the mixture. The selectivity of flophemesylamine could be particularly important in this respect.

Sensitivity of the electron capture detector can vary with temperature of the detector, depending upon the electron capture process itself⁵. The detector response to a standard quantity of dodecanol flophemesyl ether was therefore measured between 250° and 350 °C. The response increased with temperature, therefore the detector should be used at maximum operating temperature for sensitive detection of flophemesyl ethers.

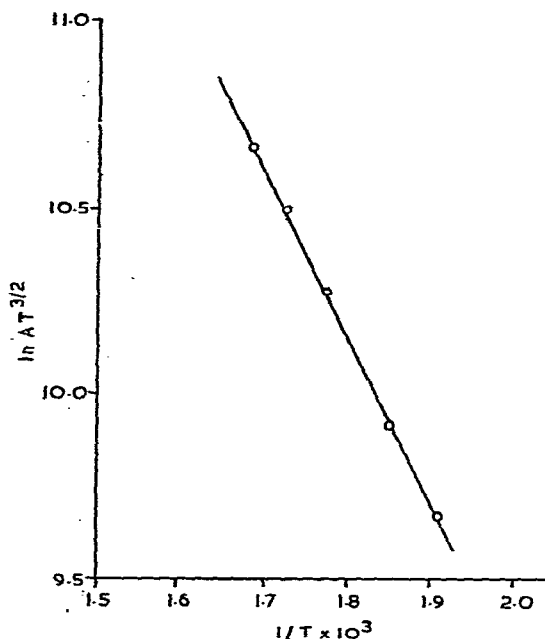
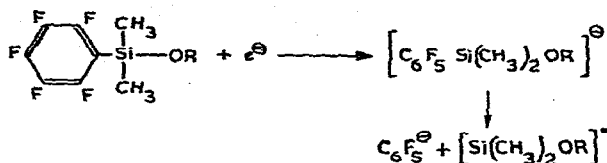


Fig. 1. Plot of reciprocal of temperature ($1/T$, $^{\circ}K^{-1}$) against $\ln AT^{3/2}$ for dodecanol flophemesyl ether to show effect of detector temperature upon detector response and negative slope of the curve.

An empirical plot of $\ln AT^{3/2}$ against $1/T$ (where A is recorder peak area for a fixed mass of compound and T is detector oven temperature in $^{\circ}K$) has been shown to reveal the type of mechanism operating during electron capture⁵. The negative slope of this curve plotted for dodecanol flophemesyl ether (Fig. 1) shows that a dissociative mechanism is operating. The pentafluorophenyl group forms a very stable anion and is a good leaving group in nucleophilic reactions in solution. The Si-O bond is relatively strong, much stronger than the Si-C bonds and the C_6F_5 group can accommodate a negative charge much more readily than CH_3 or OR. A probable mechanism is therefore:



Confirmation of this suggestion would require a plasma chromatograph⁶ or an atmospheric pressure ionization mass spectrometer⁷.

Under optimum conditions the sensitivity of detector of flophemesyl ethers of alcohols is remarkable. For example, $25 \cdot 10^{-15}$ g (25 fg) of 2,2-dimethylpropanol (neopentyl alcohol) could be detected after conversion to the flophemesyl ether, and a linear calibration curve was obtained over the range 25 fg to 2.5 pg (using pulsed ECD at 300 °C).

GC-MS of lower alcohols is very difficult, because of their poor or non-existent molecular ions and because of the large amount of interfering background at low masses. The flophemesyl ethers of simple alcohols give mass spectra characterized by a few ions, with the molecular ion always prominent, sometimes forming the base peak. This is in marked contrast to the mass spectral behaviour of the parent silane⁸. Thus butan-1-ol flophemesyl ether has M^+ 298 with other ions at m/e 283 (100%), 255, 235, 130, 79 and 77. Butan-2-ol flophemesyl ether has M^+ 298, m/e 283, 269 (100%), 225, 79, 77. *tert.*-Butanol flophemesyl ether has M^+ 298 and m/e 283 (100%), 130, 79 and 77. Neopentyl alcohol flophemesyl ether has M^+ 312 and m/e 297, 265, 255 (100%), 225, 125, 77, 57. The flophemesyl ethers therefore are well suited to determination of structure by MS or to detection by single or multiple ion monitoring. Further work on the use of flophemesyl derivatives is in progress.

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