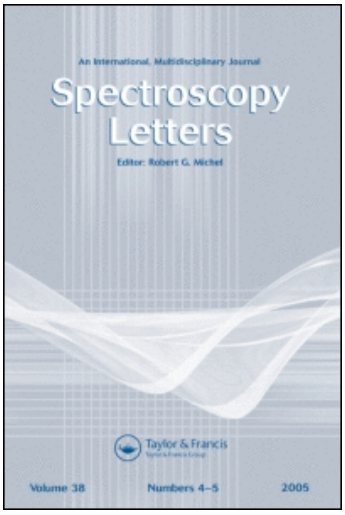

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PMR Determination of Cineole in Eucalyptus Oil

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PMR DETERMINATION OF CINEOLE IN EUCALYPTUS OIL

Key Words:

Cineole, NMR analysis; PMR analysis, Eucalyptus oil; Eucalyptol, PMR analysis; Cajeputol, PMR analysis; 1,8-Epoxy-p-Menthane, PMR analysis.

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Abstract:

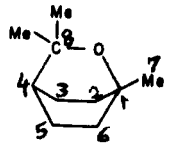
An accurate, more convenient and less time-consuming PMR procedure is described for the quantitative determination of cineole in bulk drug and in a sample of eucalyptus oil. Standard mixtures containing pure cineole showed a mean result of 100.6 ± 0.7%. The results, obtained by applying this method for the determination of cineole in eucalyptus oil, are compared with those found using the official BP method.

In addition, the PMR spectrum of cineole provides a very specific means for its identification.

Introduction:

Cineole occurs, in varying amounts, in many volatile oils and constitutes a major component of eucalyptus oil. It has many pharmaceutical and medicinal importance.

The lack of a reactive group in the cineole structure limits the chances of developing a sensitive method for its quantitation by chemical means. The official B.P. method (1) depends on the physical properties of the drug in depressing the freezing point of a mixture of cineole and o-cresol. Other methods have been reported in the literature for the determination of cineole. Some of these methods are based on the formation of an additive compound with phosphoric acid (2), arsenic acid (2) or resorcinol (3). The addition compound is then decomposed and the amount of cineole measured. Cineole has also been determined by IR and UV spectrophotometry (4,5), as well as by a colorimetric method (6).



The present study investigates the utility of the PMR spectroscopy in the quantitation of cineole as a pure entity and as a constituent of a sample of a volatile oil. The advantage of the PMR procedure over the previously reported methods are discussed.

Experimental:

Apparatus and Chemicals:

NMR spectrometer[1] was used for the analysis. Standard cineole[2], Eucalyptus oil[2] (Rectified; 80-85%) Internal standard Benzophenone[3], Carbon tetrachloride[4].

All chemical shifts reported are in reference to tetramethylsilane at o ppm.

Preparation of sample solutions:

Weigh accurately the specified amounts of sample (cineole or eucalyptus oil) into glass-stoppered weigh-

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1. Varian T-60A, 60 MHz, Palo Alto, California U.S.A.
2. Riedel de Haen A.G. Seelze, Hannover, West Germany.
3. B.D.H. Chemicals, Poole, England.
4. Koch-Light Laboratories Ltd., Colnbrook, Bucks, England.

ing flasks. Add the specified, accurately weighed, amounts of benzophenone and 2ml. of carbon tetrachloride. Stopper, shake to dissolve and transfer about 0.5ml. of each solution into precision NMR spectrometer tube and obtain the spectrum, adjusting the spin rate to eliminate the spinning side-bands as much as possible. Integrate, at least three times, the peaks of interest (C_1-methyl protons appearing at 0.98 ppm or C_8-dimethyl protons occuring at 1.17 ppm) and determine the average integral.

The amount of cineole may then be calculated using the following equation:

$$\text{mg of cineole} = \frac{A_c}{A_b} \times \frac{EW_c}{EW_b} \times \text{mg of benzophenone}$$

Where A_c = integral value of the signal representing cineole.

A_b = integral value of the signal representing benzophenone.

EW_c = formula weight of cineole /6 = 25.67 (for C_8-dimethyl protons).

or = formula weight of cineole /3 = 51.34 (for C_1-methyl protons).

and EW_b = formula weight of benzophenone /10 = 18.22

Results and Discussion:

The PMR spectrum of cineole in carbon tetrachloride (Fig. 1) shows among other peaks a very highfield singlet at 0.98 ppm attributed to its C_1-methyl protons. Although this peak does not represent the largest single area for measurement compared to the C_8-dimethyl protons singlet at 1.17 ppm it has been chosen as the area for precise integration in eucalyptus oil (Fig. 2) as it is free from any interference. On the other hand the two signals are interference-free in pure cineole and each can serve equally good for its quantitation.

Benzophenone was used as the internal standard because it provides resonance signals in a sufficiently downfield position from the cineole resonance pattern to allow for interference-free quantitation (Fig. 3). Both cineole and benzophenone dissolve in carbon tetrachloride which makes it the solvent of choice. Carbon tetrachloride offers the advantage of adding no proton signals to the spectrum.

A series of standard mixtures containing pure cineole and benzophenone in carbon tetrachloride were prepared and assayed using the PMR procedure. The results of Table I show that the method is accurate

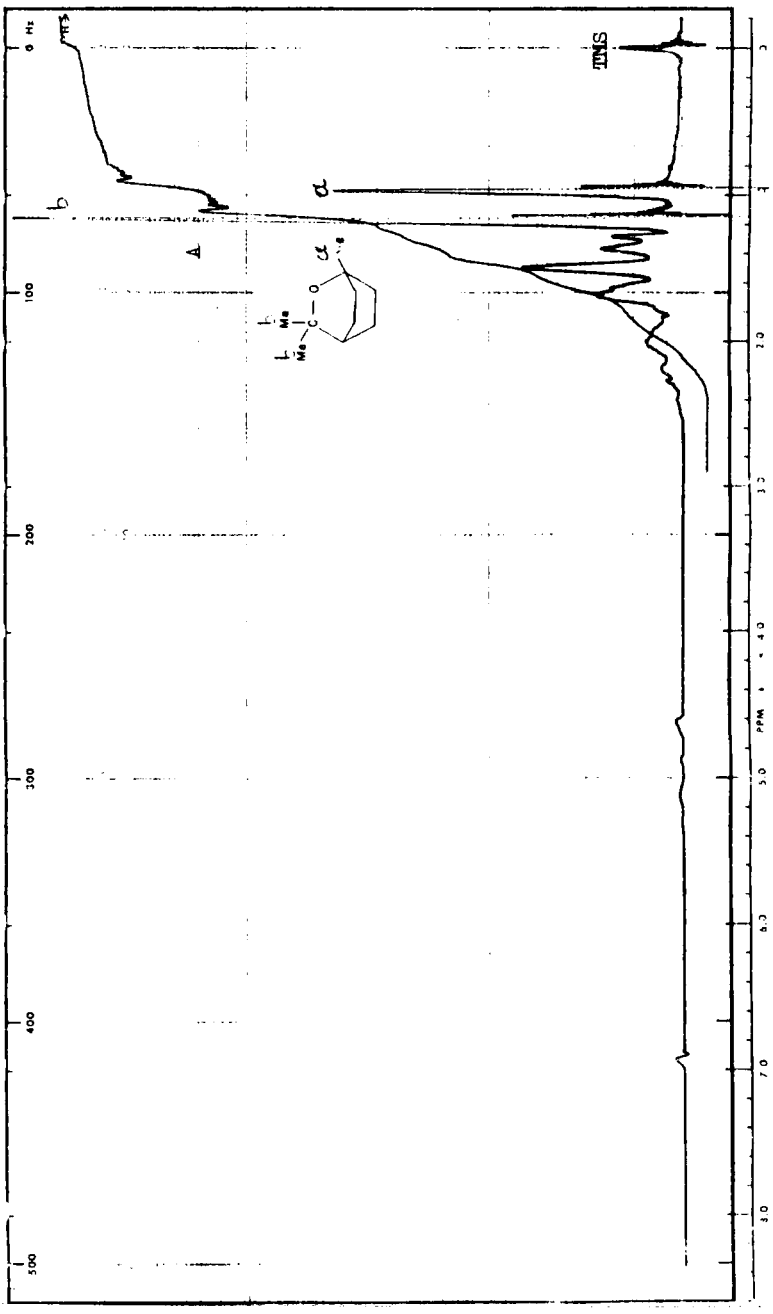

Fig. 1 - PMR spectrum of cineole (A) and tetramethyl-silane (TMS) in carbon tetrachloride.

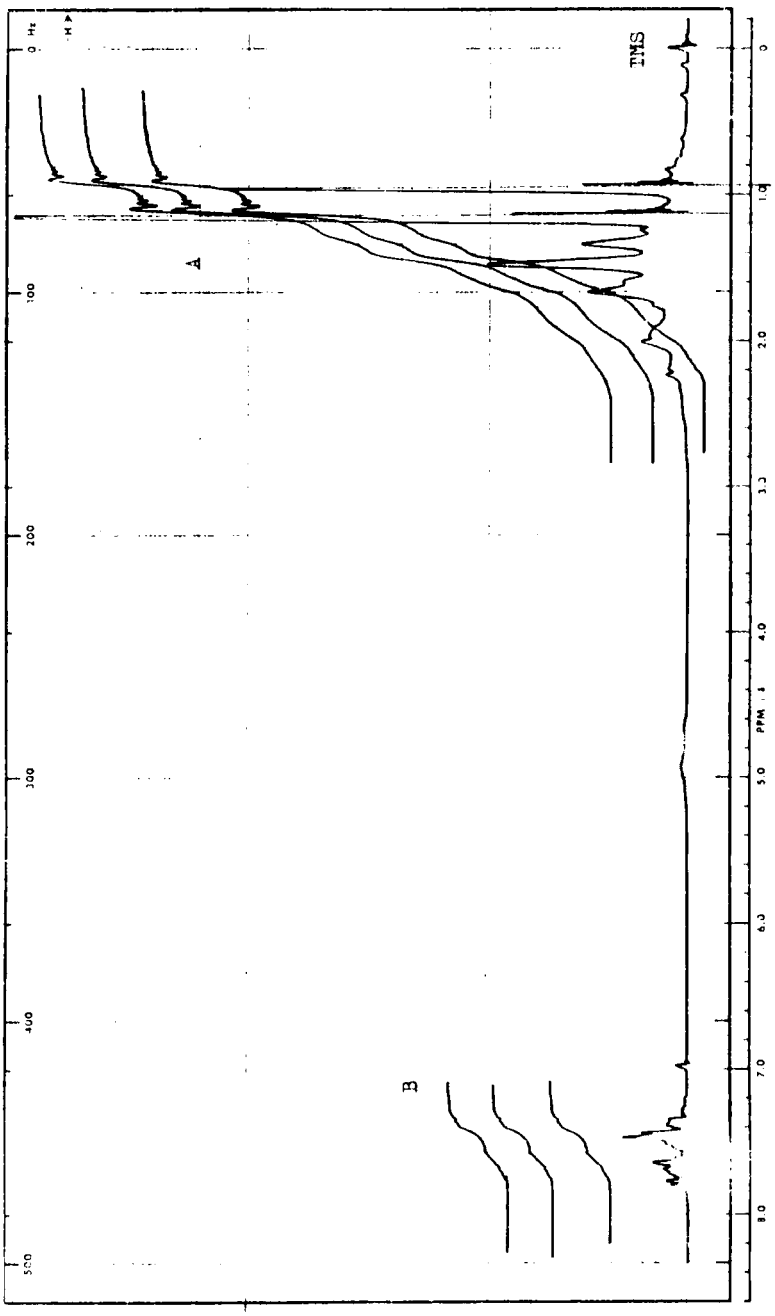

Fig. 2 - PMR spectrum of eucalyptus oil (A), benzophenone (B) and tetramethylsilane (TMS) in carbon tetrachloride.

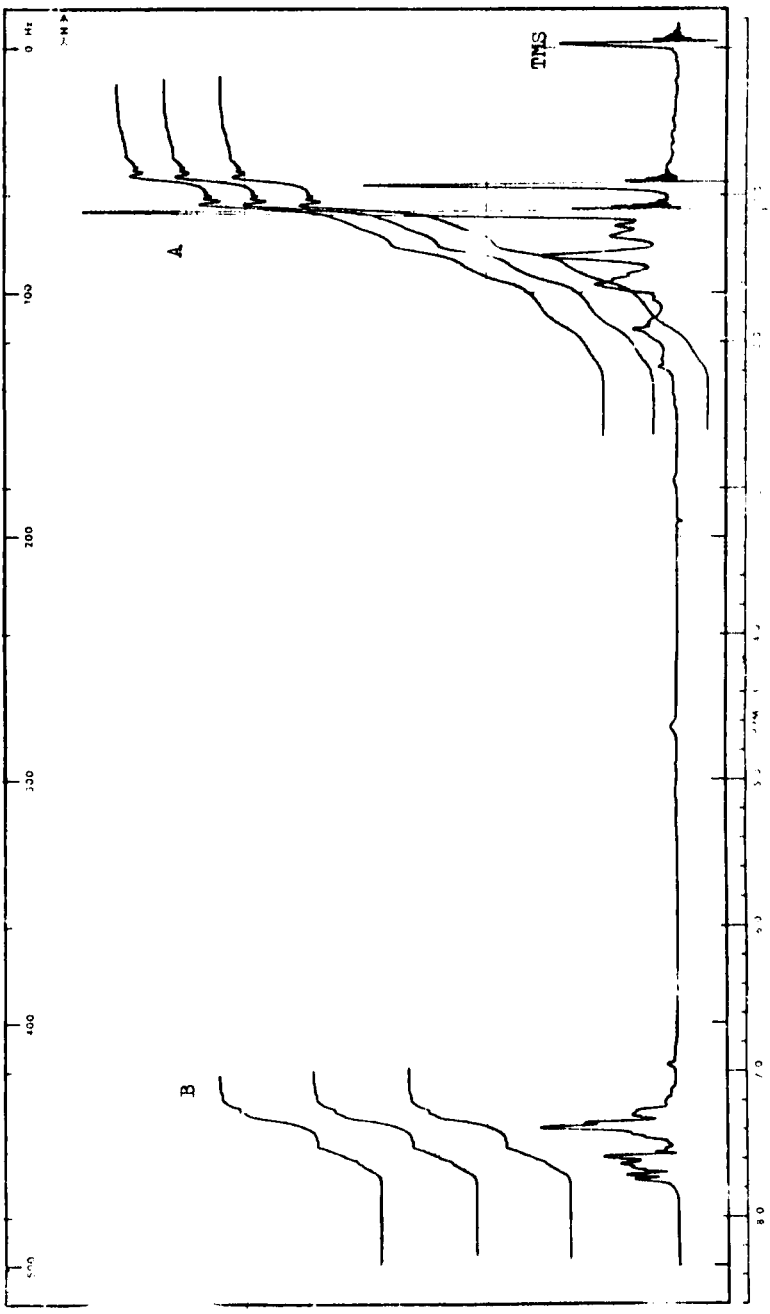

Fig. 3 - PMR spectrum of pure cineole (A), benzophenone (B) and tetramethylsilane (TMS) in carbon tetrachloride.

Table I - Determination of cineole in Standard Mixtures by PMR.

Standard Mixture	Internal Standard[a] mg.	Cineole		
		Added mg.	Found mg.	Recovery % w/w
1	50.0	50.0	50.3	100.6
2	100.0	100.0	101.3	101.3
3	150.0	150.0	150.6	100.4
4	175.0	175.0	177.3	101.3
5	200.0	200.0	203.2	101.6
6	200.0	250.0	251.7	100.7
7	200.0	300.0	298.4	99.5
8	200.0	350.0	351.4	100.4
9	200.00	400.0	399.3	99.8
			Average	100.6
			SD	± 0.7

[a] Benzophenone.

and precise with a mean recovery of 100.6 ± 0.7% calculated on the basis of either the C_1-methyl protons singlet at 0.98 ppm or the C_8-dimethyl proton singlet at 1.17 ppm.

The new procedure was also applied for the quantitation of cineole in eucalyptus oil (Table II).

Table II - Determination of cineole in Eucalyptus oil by GLC.

Sample No.	Internal Standard[a] mg.	Added amount of Eucalyptus oil mg	Cineole contents	
			mg	% w/w
1	80.0	100.0	93.7	93.7
2	80.0	200.0	186.7	93.4
3	80.0	300.0	281.6	93.8
4	80.0	350.0	331.8	94.8
5	80.0	400.0	376.2	94.1
6	80.00	80.0	75.2	94.0
			Average	93.97
			SD ±	0.48

[a] Benzophenone.

The method proved to be reproducible with a mean result of 93.97 ± 0.48%. These results are not in agreement with the stated amounts of cineole in the oil sample (80 - 85%) or with the results obtained using the official B.P. method. (Three different runs gave percent results of 80, 82 and 84 respectively).

The accuracy of the B.P. method is affected by many factors such as moisture content and other compo-

nents present in the oil and the method also requires a highly pure and dry o-cresol with a minimum freezing-point of 30° (1,2 & 7).

The PMR procedure, however, is not affected by any of the above factors. In addition it is rapid and simple like other spectroscopic methods but much more specific since its spectrum provides a unique field positions of the various protons for unambiguous identification and subsequent quantitation.

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