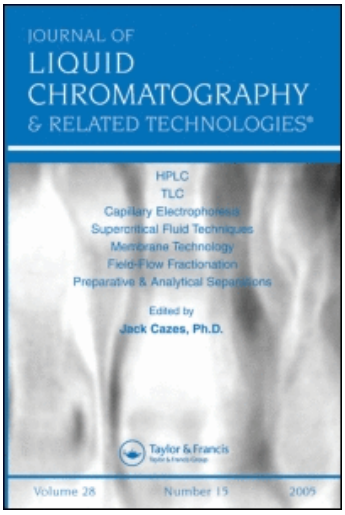

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Routine Preparative HPLC of Aromatic Silyl Compounds on Caffeine Coated on Silica Gel

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ROUTINE PREPARATIVE HPLC OF AROMATIC SILYL COMPOUNDS ON CAFFEINE COATED ON SILICA GEL

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ABSTRACT

A liquid chromatographic method using caffeine coated on silica gel, for separation and purification of acenaphthenylsilyl compounds is described. This has been achieved on a preparative scale.

INTRODUCTION

The rapid and facile separation of a few grams compounds for synthesis or analytic identification have always been the hope of the bench chemist.

When the purifications are not possible by distillation or fractionated crystallization, the used of an HPLC method is a solution which can help the chemist.

A mixture of polyaromatic hydrocarbons is easily separated on an analytic scale by reversed-phase chromatography (C_8 or C_{18}). But the transposition of the separation on a preparative scale (a few grams) is not possible because of the poor solubility of the polyaromatic hydrocarbons in the reversed phase eluents. The introduction of a trimethylsilyl group to the

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aromatic hydrocarbons as a substituent increase its insolubility. For a mixture of trimethylsilyl-1 acenaphthene and acenaphthene, our experiments show that 300 mg is the highest quantity that we can separate (1). It would not be an interesting way.

In fact in this example we have to separate two aromatic compounds so that a donor-acceptor chromatography appeared to be the best way to resolve the problem because the eluents (hexane) are solvents for acenaphthenyl compounds.

For the separation of polyaromatic hydrocarbons Lam used caffeine as acceptor (2-4) and Krasnec pointed out that the caffeine forms one of the strongest donor-acceptor complexes (5). On an other hand in T.L.C. caffeine is totaly retained with dry hexane as eluent, whereas acenaphthenyl compounds are eluted. So we used caffeine coated on silicagel to separate our compounds.

EXPERIMENTAL

Apparatus

a) Préparative LC : the apparatus consisted of a Chromatospac Prep 10, Jobin-Yvon system equipped with a Gilson holochrom H.M. The following samples were injected directly on the column by means of a syringe.

b) General equipment : The NMR spectra were recorded on a Perkin-Elmer R 24 B spectrometer. Results are reported in the δ scale in parts per million (ppm) with methylene chloride as internal standard (5,15 ppm down field from TMS).

The gas chromatographic analyses were performed on an Intersmat I.G. C 120 with a flame -ionization detector equipped with a

1,5 meters x 1/8 inch SE 30 10 % on chromosorb PAW column. Gas carrier was nitrogen with a flow rate of 25 ml/mn.

Reagents

Caffeine, acenaphthene, acenaphthylene were purchased from Aldrich chemical, caffeine and acenaphthene were used without further purification.

Acenaphthylene was recrystallizated from methanol.

Aceton and hexane (Aldrich Chemical) were dried on molecular sieves.

The silyl acenaphthene compounds were synthetized by procedure published earlier (6).

Silica gel is Lichroprep Si 60 (5 - 20μ) from Merck.

PROCEDURES

50 g of caffeine were dissolved in one liter of dry acetone. After dissolution 250 g of silica gel were added and mixed. The solvent was evaporated with a rotary evaporator and caffeine silica gel (20 % in weight) was activated at 80°C during 12 hours.

A 200 g amount of caffeine-silica gel were mixed with 400 ml of dry hexane and they were packed into the column (40 mm-I.D.) until the excess of hexane get out. The height of the bed was 270 mm.

Results and Discussion

a) Tests of the column

In a first time we have studied the chromatographic caracteristics of the column to know its maximum of efficiency. So we have to determinate on optimun packing pressure (pressure on

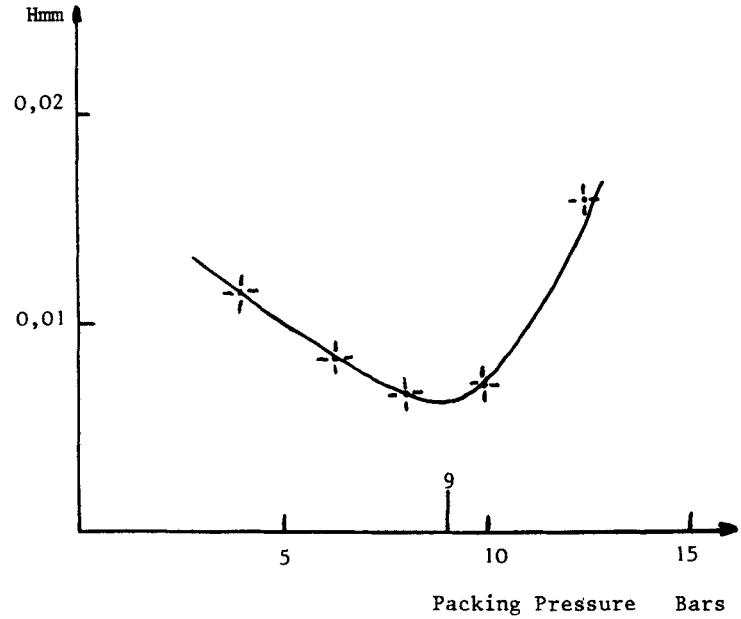

Figure 1. Variation of HETP vs packing pressure
Flow rate 30 ml/mn

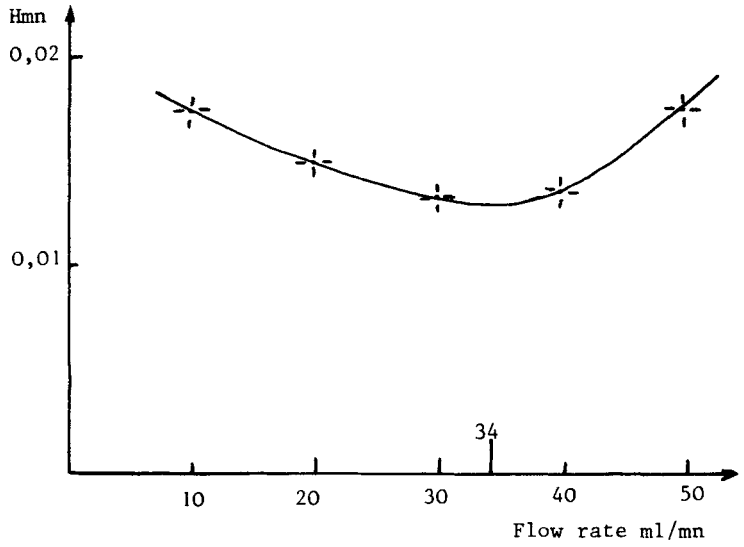

Figure 2. Variation of HETP vs flow rate
packing pressure 8.5 bars.

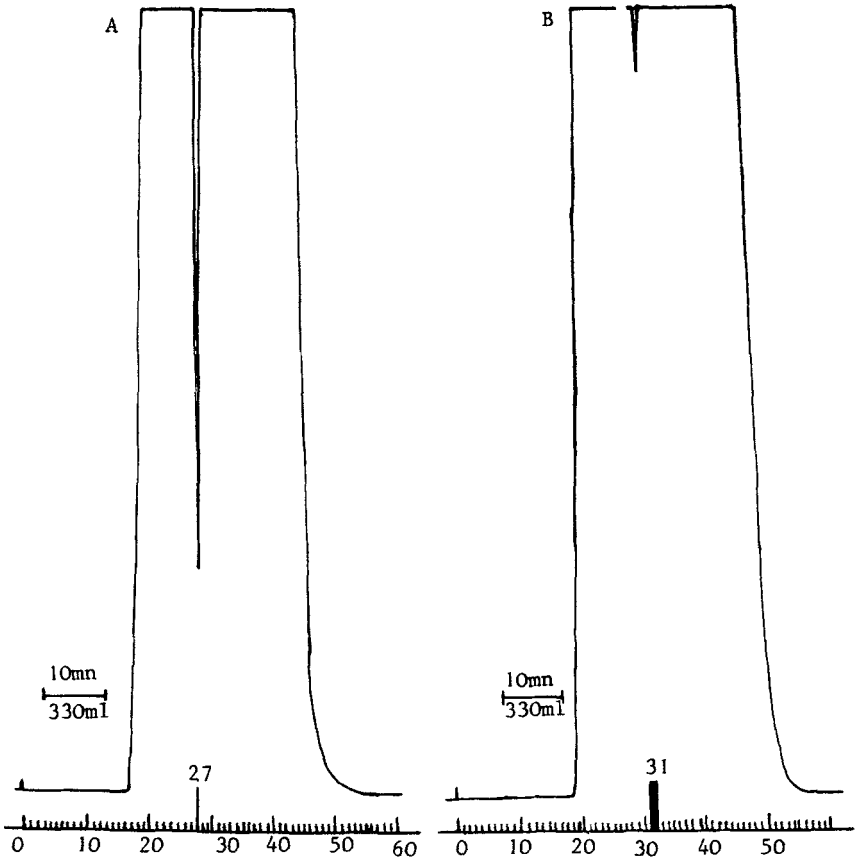

Figure 3. Separation of acenaphthene and acenaphthylene eluent dry hexane. λ = 254 nm.
(A) 2 g injected in 20 cc of dry hexane.
(B) 2,5 g injected in 25 cc of dry hexane.

the piston) and the best flow rate. These tests were made with acenaphthene (1 ml of a solution of 100 mg in 10 cc of hexane). The results are given on figures 1 and 2 : packing pressure : 9 bars, flow rate : 34 ml/mn respectively. The figure 1 shows that it is preferable to have a pressure on the piston who

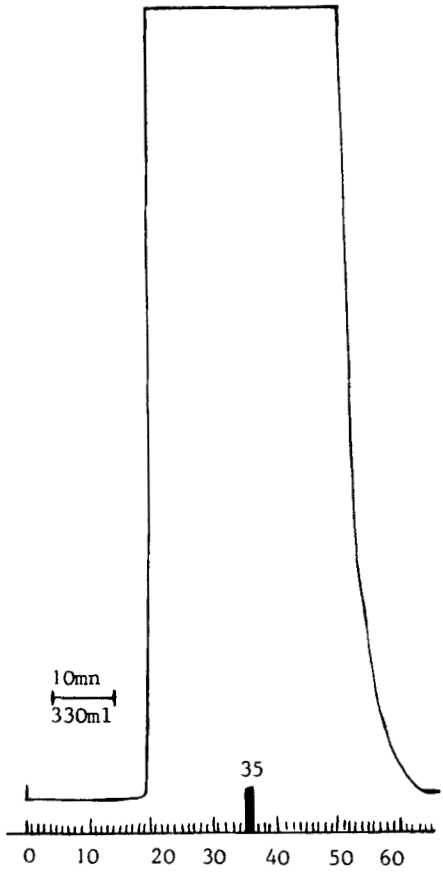

Figure 4. Separation of acenaphthene and acenaphthylene : eluent dry hexane λ = 254 nm
3 g injected in 30 cc of dry hexane

stay in the first part of the curve. So we selecte 8.5 bars. For the flow rate we choose a value of about 34 ml/mn.

Secondly we studied the capacity of the column. For that we choose to separate a synthetic mixture of acenaphthene and acenaphthylene (50/50 W/W) they are respectively white and yellow and it is easy to see observe its separations,

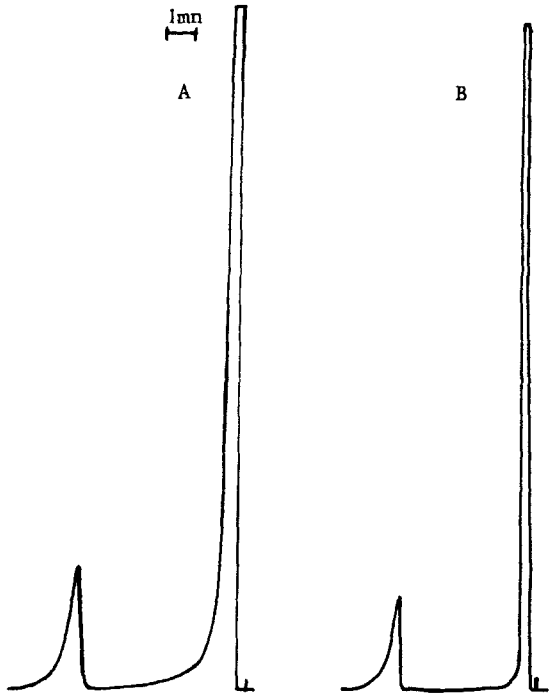

Figure 5. GC analysis: 2 g injected Temp 190°C
(A) fraction 26 acenaphthene
(B) fraction 27 acenaphthylene

in particular when the UV spectrometer is overgained (7). So that we did not oblige to analyse a lot of fractions.

Figure 3 shows that for 2 g : pure products are obtained (GC fig 5) ; for 2,5 g fraction 31 is mixed and contains less than 0,05 g of mixture (GC fig 6). The maximum of mixture that we can separate on this column is 3 g (fig 4). Only fraction 35 is mixed and contains 0,1 g of mixture (fig 7). The combined fractions 20 to 34 are acenaphthene (1,40 g) and 36 to 40 are acenaphthylene (1,35 g). The difference of 0,15 g

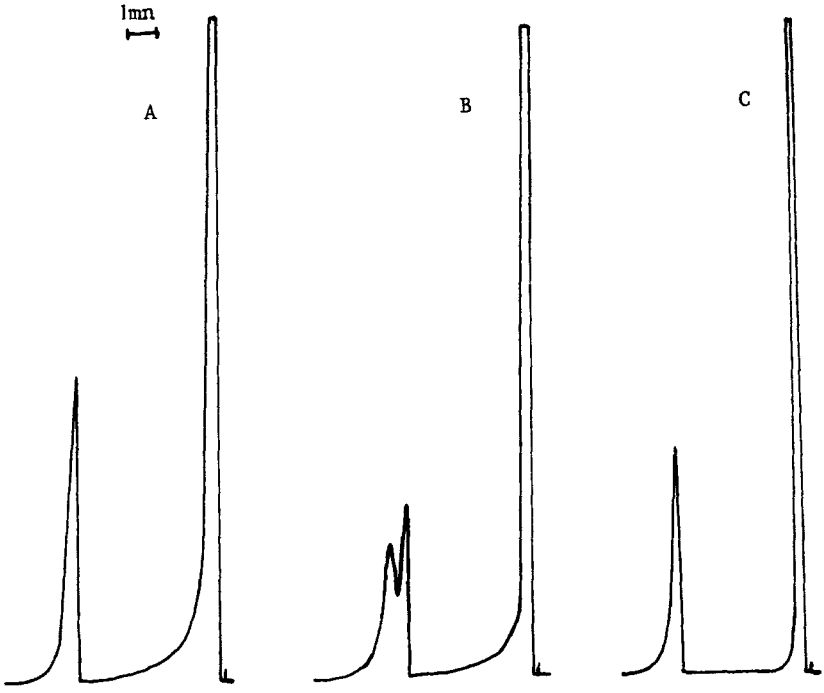

Figure 6. GC analysis 2,5 g injected Temp 190°C
(A) fraction 30
(B) fraction 31
(C) fraction 32

is due to losses in the injection and oxydatives species in acenaphthylene which stay at the top of the column.

In any fraction we did not find caffeine.

b) Purification of silylacenaphthene compounds

These studies were followed in this manner:

1) the GC analysis of the mixture, 2) the preparative chromatogram of the mixture and 3) the GC analysis of the fractions which contain the silyl compound and its NMR analysis.

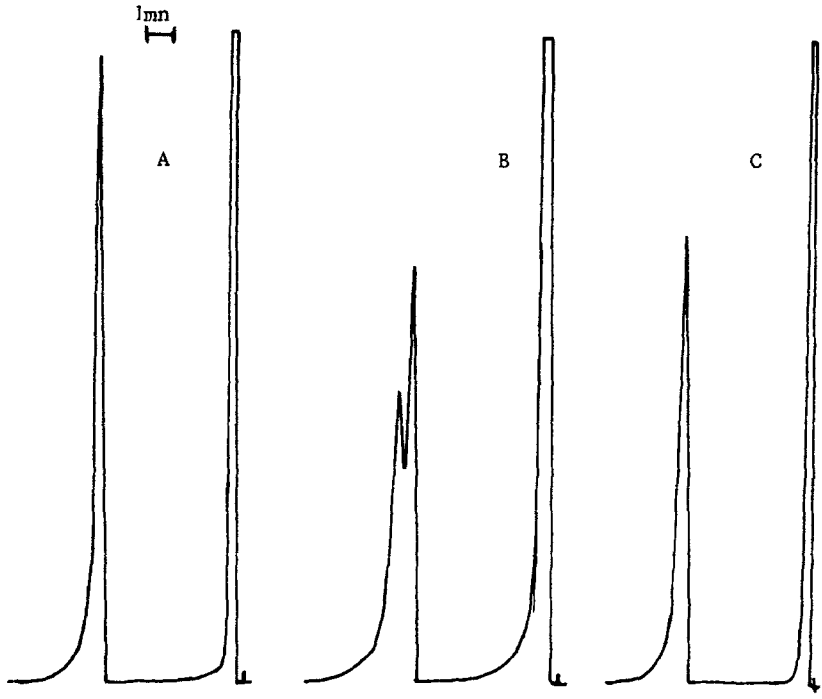

Figure 7. GC analysis 3 g injected Temp 190°C
(A) fraction 34
(B) fraction 35
(C) fraction 36

1-(trimethylsilyl) acenaphthene : this compounds is a mixture which contents about 10 % of impurities (acenaphthene, acenaphthylene and bis(acenaphthenyl-1) tetramethyldisiloxane (fig.8). The preparative chromatogram of 2,5 g is showed on figure 9.

The first fraction (14-15) contains the siloxane. The two acenaphthenyl groups of this compound are not able to form good charge - transfer with caffeine. The siloxane chain gives to the molecule a polarity less strong than the $SiMe_3$ group. So it was eluted

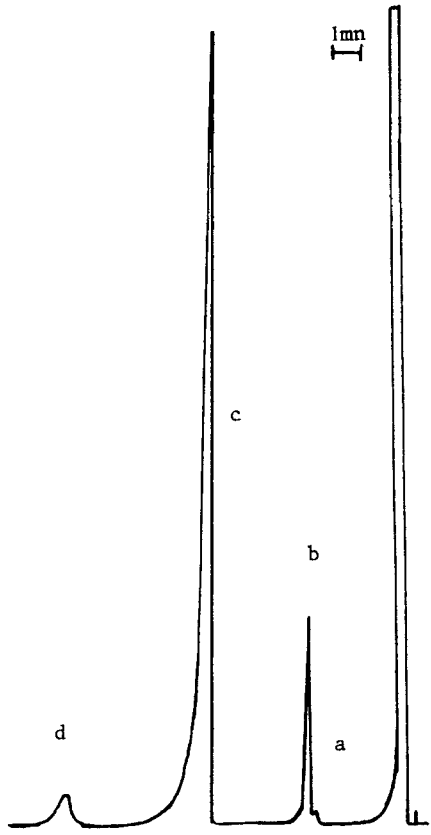

Figure 8. GC analysis of crude 1-(trimethylsilyl) acenaphthene temp 190°C
a) acenaphthylene b) acenaphthene c) 1-(trimethylsilyl)acenaphthylene d) bis(acenaphthenyl-1) tetramethyldisiloxane.

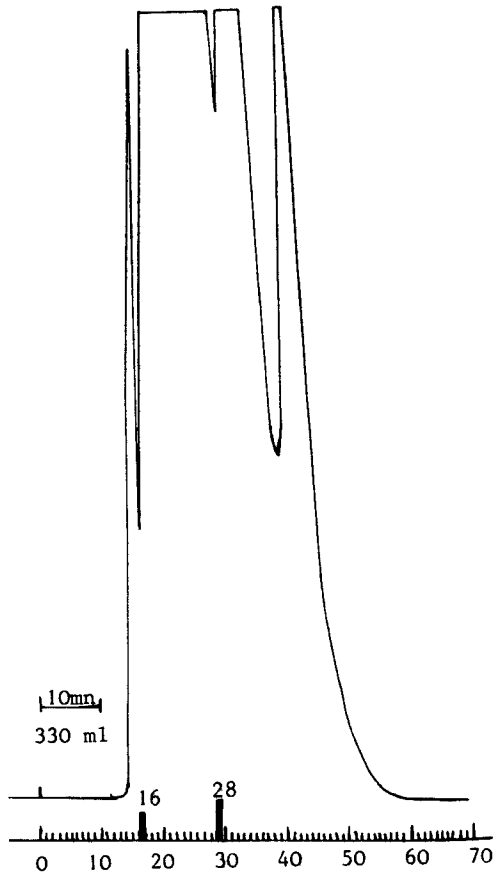

Figure 9. HPLC preparative chromatogram of crude 1-(trimethylsilyl) acenaphthene separation. λ : 254 nm.

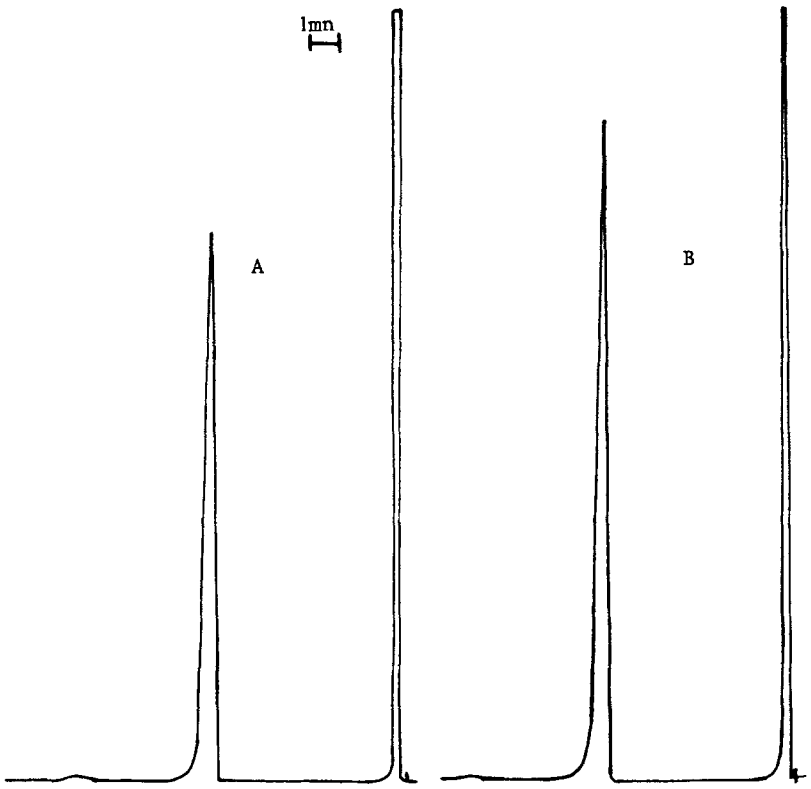

Figure 10. GC analysis of fractions of the separation of 1-(trimethylsilyl) acenaphthene Temp 190°C
(A) fraction 16
(B) fraction 17

first. The second product is the trimethylsilylacenaphthene. The figures 10 and 11 show the purity of the differents fractions examined by GC. If we take out fractions from 17 to 29 we obtained 2,3 g of pure product (NMR fig. 12). Fractions 29-40 contain acenaphthene and fractions 40-55 acenaphtylene respectively.

1-(dimethylsilyl)acenaphthene : the purity of this mixture is better than 95 % (fig. 13). The same impurities were found by GC

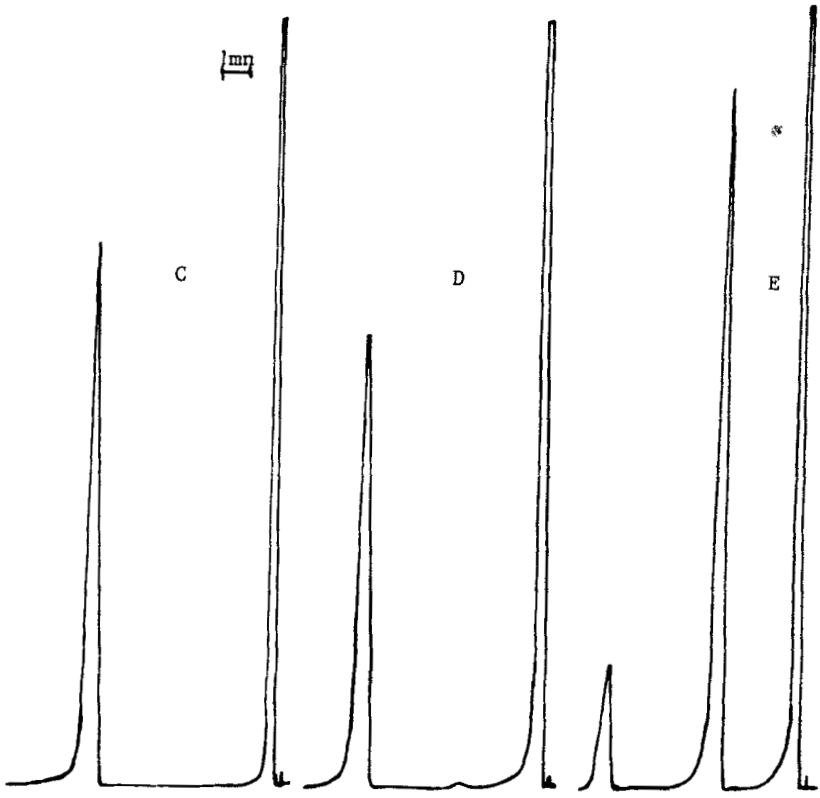

Figure 11. GC analysis of fractions after HPLC separation of 1-(trimethylsilyl) acenaphthene Temp 190°C

(C) combined fractions 18-25
(D) fraction 27
(E) fraction 28

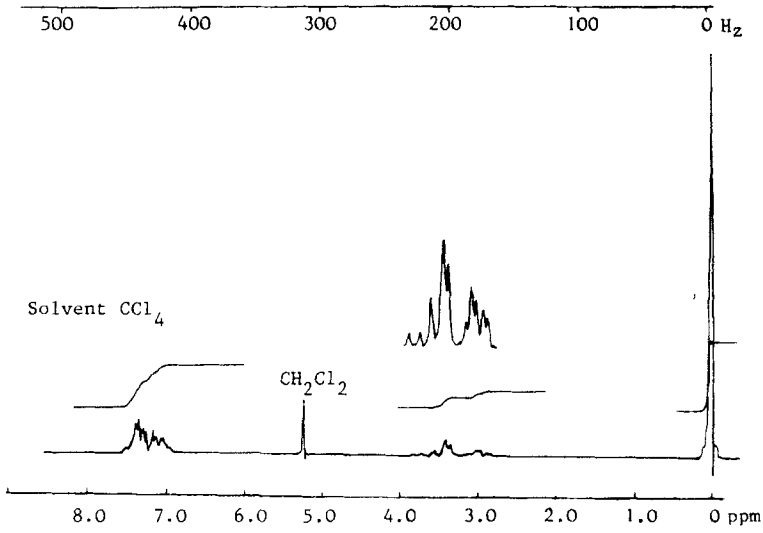

Figure 12. NMR of combined fractions 18-25. 1-(trimethylsilyl) acenaphthene

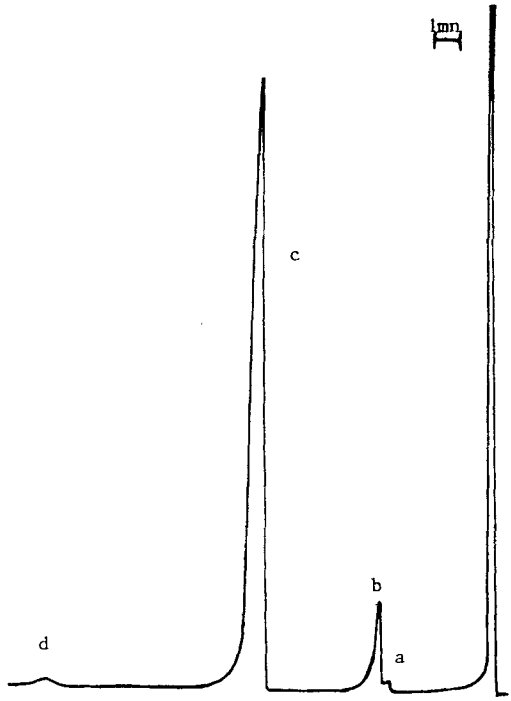

figure 13. GC analysis of crude 1-(dimethylsilyl)acenaphthene
Temp 170°C
a) acenaphthylene, b) acenaphthene, c) 1-(dimethylsilyl) acenaphthene d) bis(acenaphthenyl-1)tetramethyldisiloxane.

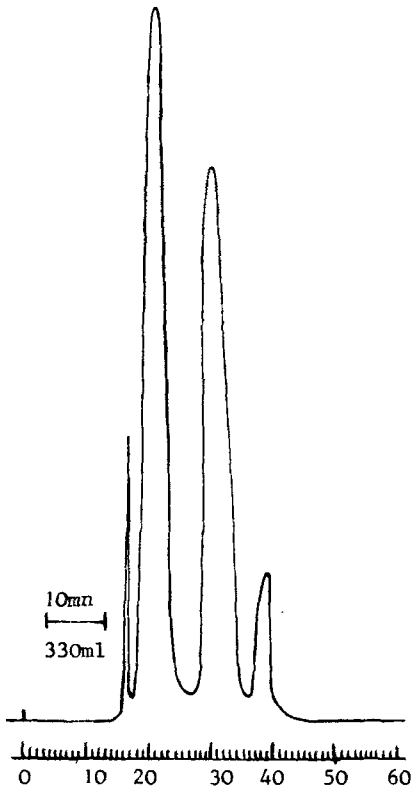

Figure 14. HPLC preparative chromatogram of crude 1-(dimethylsilyl)acenaphthene separation. λ = 320 nm

as for 1-(trimethylsilyl)acenaphthene. The quantity injected was 1 g ; so we obtained one chromatogram directly analysable (fig 14). Fractions 15-16 are the siloxane, fractions 18 to 25 contain 0,9 g of the silane which is obtained with an excellent purity (fig. 15). Fractions 28-35 are acenaphthene, and fractions 37-42 acenaphthylene.

The NMR spectrum (fig. 16) shows that the methyl groups in the Me_2HSi moiety are not in the same environnement. One of

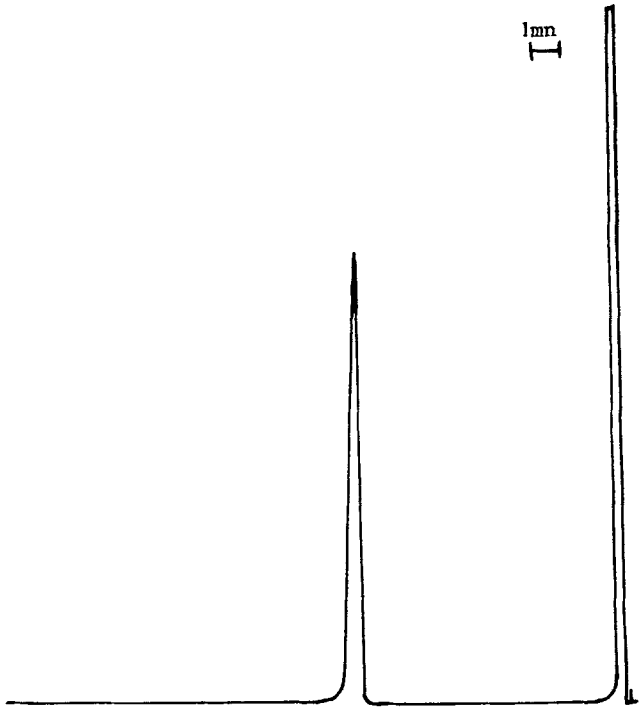

Figure 15. GC analysis of combined fractions 18-25 of 1-(dimethylsilyl)acenaphthene
Temp 170°C

them is in the shelding aera of the cycle, the other is out: so we have four signals.

In our studies we didn't find caffeine in any fraction if we used dry solvents. If we used solvents saturated with water we have been able to eluete caffeine. We found about 100 mg of caffeine by gram of injected product. In the case it is preferable to use 7-(2,3 dihydroxypropyl)theophylline (8) than caffeine.

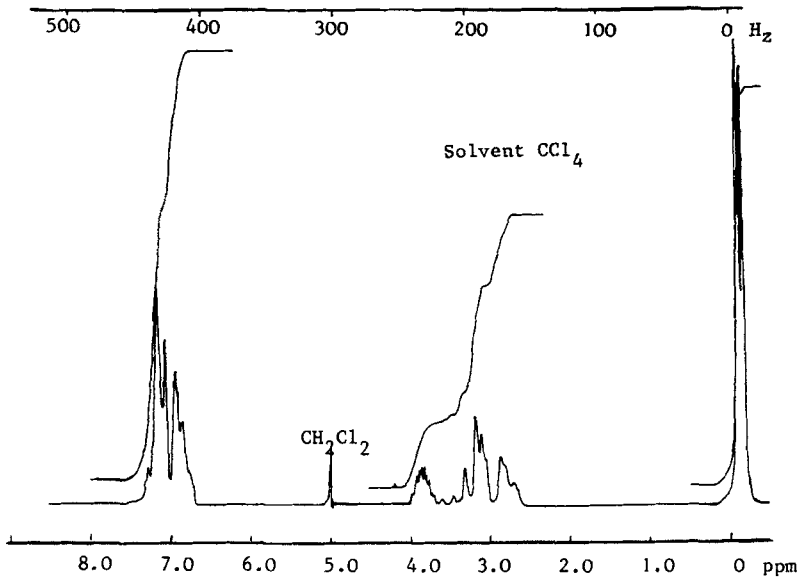

Figure 16. NMR of combined fractions 18-25 of 1-(dimethylsilyl)acenaphthene

Conclusion

Preparative HPLC on silica gel coated with caffeine has been found to be a good method for the separation of silylacenaphthenyl mixtures resulting in high yield of the silyl compounds having excellent purity.

References

1. For the separation : 200 g Lichroprep RP8 15-25 µ; Packing Pressure 10 bars ; eluents Methanol/water, 80/20 ; flow rate 30 ml/mn ; quantity injected : 300 mg in 30 ml of methanol.

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7. Our Gilson HM spectrometer is equipped with a cell of 50 µl and 3 mm of optic way it have a maximum D.O. of 2.

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