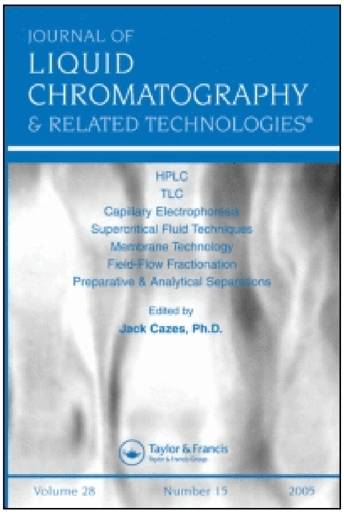


Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

Preparative HPLC of Indole Silyl Compounds on 3,5-Dinitrobenzamide Silica Gel

Cécile Bertrand[a]; Guy Félix[a]; Claude Biran[a]; Michael Fourtinon[a]
[a] Laboratoire de Chimie Organique et Organométallique CNRS UA 35, Université de Bordeaux I, Talence Cedex, France

To cite this Article Bertrand, Cécile , Félix, Guy , Biran, Claude and Fourtinon, Michael(1987) 'Preparative HPLC of Indole Silyl Compounds on 3,5-Dinitrobenzamide Silica Gel', Journal of Liquid Chromatography & Related Technologies, 10: 5, 853 — 861

To link to this Article: DOI: 10.1080/01483918708066740

URL: http://dx.doi.org/10.1080/01483918708066740

JOURNAL OF LIQUID CHROMATOGRAPHY, 10(5), 853-861 (1987)

PREPARATIVE HPLC OF INDOLE SILYL COMPOUNDS ON 3,5-DINITROBENZAMIDE SILICA GEL

Cécile Bertrand, Guy Félix*, Claude Biran,
and Michael Fourtinon
Laboratoire de Chimie Organique et Organométallique
CNRS UA 35
Université de Bordeaux I,
351, Cours de la Libération
33405 Talence Cedex, France

ABSTRACT

The use of a preparative charge-transfert liquid chromatography for the separation of 1,4- and 1,5-bis(trimethylsilyl)indole isomers on 3,5-dinitrobenzamide silica gel is reported and discussed.

INTRODUCTION

In a previous paper, we reported our studies on the separation of aromatic silyl compounds in preparative HPLC by π comlexing phases (1). As an extention of this work we wish to report the successful separation of 1,4-bis(trimethylsilyl)indole and 1,5-bis(trimethylsilyl)indole as well as of 4-trimethylsilyl indole and 5-trimethylsilyl indole by donor-acceptor chromatography, both on analytical and preparative scale.

Several authors (2) have shown that silica gels coated with acceptors are suitable phases for the separation of aromatic and heterocyclic compounds. We used successfully caffeine coated on silica gel for the separation of acenaphthenyl silyl compounds (1). However, with water-containing solvents this coated phase is not suitable because caffeine is slowly eluted during the separation. One way to over come this difficulty is to achieve the separation on a chemically bonded phase. For this purpose, we synthesized a 3,5-dinitrobenzamide bonded phase*which is particularly convenient for the separation of aromatic compounds (3).

EXPERIMENTAL

double pump HPLC, equipped with a Rheodyne 7010 injection valve (10 µl sample loop) and an L.D.C. Spectro Monitor III containing a variable wavelenghth U.V. detector.

The analytical column (250 x 4.6 mm) of 3,5 dinitrobenzamide phase (10 µ) has been described earlier (3).

c) NMR spectrometer : The NMR spectra were recorded on a Perkin-Elmer R 24 B Spectrometer. Results are reported on δ scale in parts per million (ppm) with TMS as an internal standard.

Reagents

- Silica gel was Lichroprep Si 60 25-40 μ from Merck.

- The silyl indole compounds were synthesized following the reference 4.

Procedure

The preparation of the 3,5-dinitrobenzamide phase (from aminopropyl phase and 3,5-dinitrobenzoyl chloride) has been achieved as for the analytical column (3).

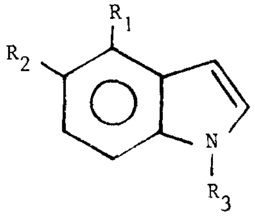
A 200 g amount of 3,5 dinitrobenzamide silica gel were mixed with 400 ml of hexane and the mixture was packed into the column (40 mm I.D.). After excess of hexane was removed, the height of the bed was 300 mm.

RESULTS AND DISCUSSION

The separation of the trimethylsilylindole compounds on a reversed phase columns is quite good. But the organic silyle compounds are hydrophobic; there are insoluble in water, alcohol and acetonitrile so the separation on a preparative scale by reversed phase chromatography is not possible.

a) Analytical separation

The separation of the crude (Fig. 1a) or recrystallized (Fig. 1b) isomers was performed on analytical scale. The different isomers were identified by ^{1}H NMR after separation of the recristallized mixture.



A : $R_1 = R_2 = H$; $R_3 = SiMe_3$

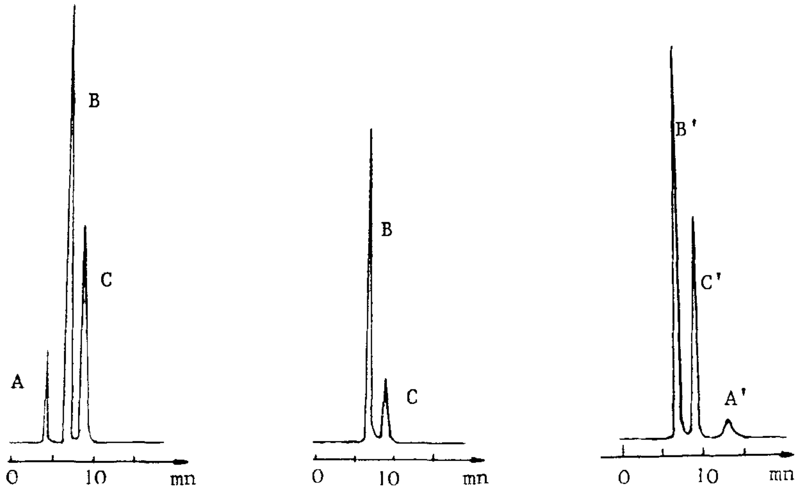
B : $R_1 = R_3 = SiMe_3$; $R_2 = H$

C : $R_2 = R_3 = SiMe_3$;$R_1 = H$

A': $R_1 = R_2 = R_3 = H$

B': $R_2 = R_3 = H$; $R_1 = SiMe_3$

C' : $R_1 = R_3 = H$; $R_2 = SiMe_3$



eluent	hexane	hexane	hexane/CH_2Cl_2-70/30
flow rate	0.7 ml/mn	0.7 ml/mn	1 ml/mn
UV detection	λ = 254 nm	λ = 254 nm	λ = 254 nm

a) Original mixture b) After recristallization c) After cleavage with MeOH

Figure 1

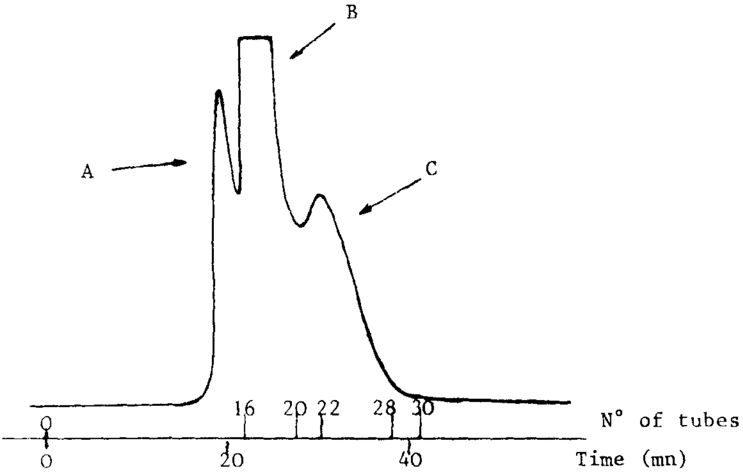


Figure 2 : 0,5 g Sample size monitored at λ = 290 nm eluent, hexane ; flow rate : 20 ml/mn

Separation of 4-trimethylsilyl indole (B') and 5-trimethylsilyl indole (C') which were obtained from a mixture of bis-trimethylsilyle indole isomers (B, C) after cleavage by methanol (6) was shown (Fig. 1c).

b) Preparative separation

The chromatographic caracteristics of the column were first studied to reach its maximum efficiency. Optimum packing pressure and flow-rate were established using N-trimethylsilyl indole (1 ml of a solution concentration 10 mg/ml) as a testing sample.

The maximum HETP was reached for a Packing pressure of 5.4 bars and a flow rate of 10 ml/mn. We use UV detection at 290 or 310 nm.

1) 0,5 g sample size

After this preliminary study we achieved the separation of the bis-trimethylsilyl indole isomers first on a small scale. Fractions 12-16 contained only isomer A. Fractions 17-19 contains

Table 1: Mixture composition

	injection	A	B	C	B+C	A'	B'	C'	Total recovery
Isocratic	2 g	0.1	0.5	0.2	0.2	0.8			1.8 g
Pseudo-gradient	3 g	0.3	0.7	0.3	0.4	0.1	0.7	0.4	2.9 g

pure B and fractions 22-27 pure C. Fractions 20 and 21 contains a mixture of B and C (Fig. 1). Only 250mg were recovered.

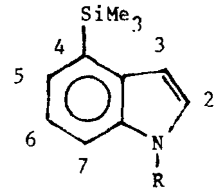
2) 2 g sample size

With a two grams sample we could make a more real approach of the problem. Only 50 % of the sample was recovered. The other 50 % was released by washing the column with methylene chloride and identified as a mixture of trimethylsilyl indoles (A' + B' + C' - Table I). In fact the residual silanol groups on the silica gel are probably enough acidic to cleave the nitrogen-silicon bond. The reaction of the sily-nitrogen compounds is well know and used to graft silica with the maximum of carbon content (7).

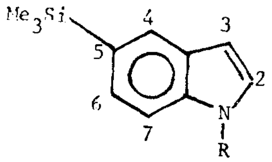
3) "Pseudo-gradient" on 3 g sample size

To solve this problem of recovering the maximum amount of products, we used a "pseudo gradient" by replacing hexane with a mixture of hexane/methylene chloride 70/30 v/v after the elution of pure C isomer. The results of the separation are shown in Figure 2 and the quantity of recovered product in Table 1. The NMR date of the pure fractions are shown in Table 2.

A



B



		H$_2$	H$_3$	H$_4$	H$_5$	H$_6$	H$_7$	C SiMe$_3$	N SiMe$_3$	NH
R = SiMe$_3$	A	7.15 dd ; J = 3.5 Hz	6.68 dd ; J = 3.5 Hz		7.25 m	7.12 m	7.47 m	0.38 s	0.53 s	
	B	7.14 dd ; J = 3.2 Hz	6.59 dd ; J = 3.2 Hz	7.84 s		7.34 m	7.50 m	0.30 s	0.53 s	
R = H	A	7.20 dd ; J = 8.7 Hz	6.68 dd, J = 8.7 Hz		7.29 m	7.23 m	7.40 m	0.41 s		8.5–8.5 m
	B	7.21 dd ; J = 3.2 Hz	6.61 dd ; J = 3.2 Hz	7.85 s		7.25 m	7.40 m	0.32 s		7.9–8.3 m

Table 2 : ^{1}H NMR date of bis(trimethylsilyl)indole isomers

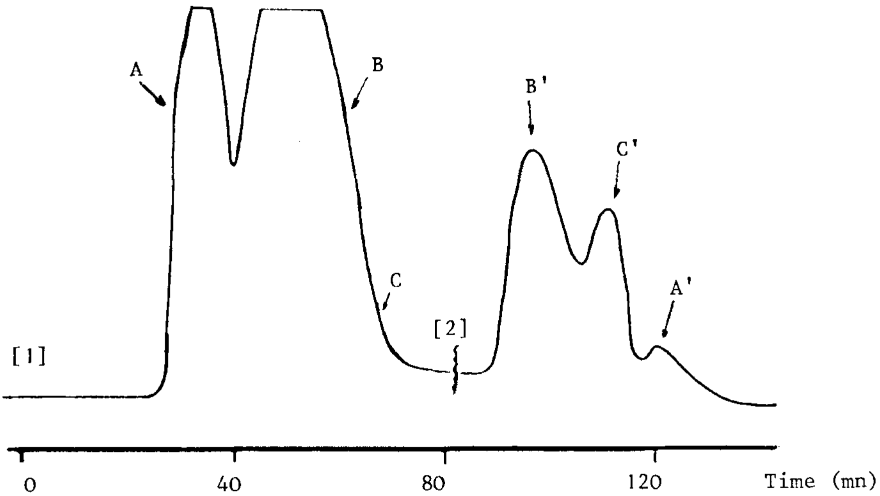


Figure 3 : Pseudo-gradient monitored at 310 nm.
eluent : [1] hexane ; [2] hexane/CH_2Cl_2 - 70/30 V/V
Flow rate 10 ml/mn

CONCLUSION

The separation of isomeric bis(trimethylsilyl) indoles has been achieved on a preparative scale. The use of charge - transfer chromatography appeared to be a good technic for the separation of organic aromatic and heterocyclic compounds because it resolve the problem of the solubility of the samples in the eluents and permit preparative scale.

REFERENCES

1. G. Félix, C. Bertrand, A. Février, J. Liquid.Chromatogr. 7, 2383(1984).

2. For review, see : W. Holstein, H. Hemetsberger, Chromatographia 15, 186 (1982).
3. G. Félix, C. Bertrand, High Resolution Chromatogr. & Chromatogr. Commun. 7, 714 (1984).
4. C. Biran, B. Efendene, J. Dunoguès, J. Organomet.Chem. 253, C13 (1983).
5. A.G.M. Barrett, D. Dauzonne, D.J. Williams, J.Chem.Soc.Chem. Commun. 637 (1982).
6. A.G.M. Barrett, D. Dauzonne, J.A. O'Neil, A. Renaud, J.Org.Chem. 49, 4409 (1984).
7. K. D. Lork, K.K.Unger, J.N. Kinkel, J.Chromatogr. 352, 199(1986).