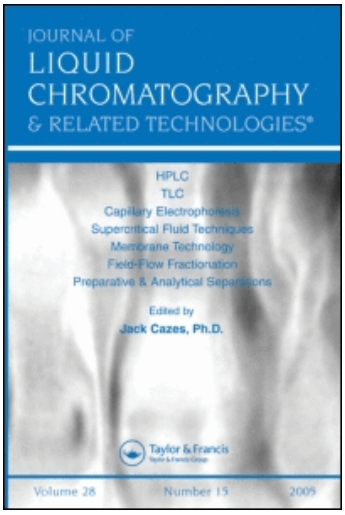

Journal of Liquid Chromatography & Related Technologies

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

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To cite this Article Shalaby, A. , Budvári-Bárány, Zs. , Szasz, Gy. , Hankó-Novák, K. and Hermecz, I.(1985) 'Adsorption HPLC Investigation of Nitrogen-Bridged Compounds', Journal of Liquid Chromatography & Related Technologies, 8: 2, 381 — 386
To link to this Article: DOI: 10.1080/01483918508067085
URL: http://dx.doi.org/10.1080/01483918508067085

JOURNAL OF LIQUID CHROMATOGRAPHY, 8(2), 381-386 (1985)

ADSORPTION HPLC INVESTIGATION OF NITROGEN-BRIDGED COMPOUNDS

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ABSTRACT

Twenty two of tricyclic nitrogen bridged derivatives were examined by HPLC method in Zorbax SIL/chloroform--methanol system. Relationship between chemical structure (ring size, ring sequence, position of methyl substitution) and chromatographic behaviour is discussed.

INTRODUCTION

We have earlier studied various physical and chemical properties of nitrogen-bridged compounds /1,2,3/. Relationships have been demonstrated between the structures and the GC and TLC behaviour of these compounds /4/. Reversed--phase HPLC studies have also been carried out on the same structural types with two and three rings /5/, and

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a relationship has been established between the HPLC behaviour and the chemical structure /6/.

These compounds display a definite polarity, mainly due to the basic N(1) atom and the C(4)=O group. The pK ranges between 2.2 and 4.4. As a consequence of the characteristics interactions, a stationary phase may be predicted between these compounds and silica gel. A study of their adsorptive (HPLC) behaviour seemed an interesting task form both theoretical and practical aspects.

Ayyangar and Srinivasan /7/ have studied the bahaviour of some acetanilide analogues (pK from 1.2 to 2.8) in an adsorption HPLC system. The retention of these compounds depended on their basicity: the compound with the strongest basicity had the highest k' value. A quantitative relationship was established for the 17 compounds tested. Similar behaviour would have been expected for our tricyclic pyrido-pyrimidine model substances (having pK values from 2.2 to 4.6 see Table 1). However, the k' values clearly demonstrate that the elution order does not follow the sequence of basicity. The retention depends appreciably on structural factors such as the ring size, the nature and positions of the substituents, i.e. the actual electron distribution, steric effects, etc.

EXPERIMENTAL

Materials

All the model substances were synthetized in our laboratory; their identification and quality control were performed via melting point determination and chromatography.

All chemicals and solvents were of analytical grade (Merck), and were used without further purification.

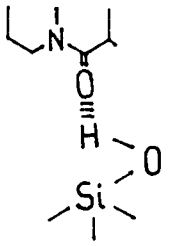
Chromatography

The HPLC apparatus was a LIQUOCHROM Model 2010 (LABOR MIM, Budapest, Hungary). A variable-wavelength detector was used, and the column effluent was monitored at different wavelengths between 270 and 330 nm. The Zorbax SIL column measured 250 x 4.6 mm and was prepacked with material with a particle size of 5 μm (DuPont). 20 μl of sample solution (0.1 mg/ml in methanol) was injected. Mobile phase: chloroform-methanol 99:1. Flow rate: 1.0 ml/min All experiments were run at 25 °C.

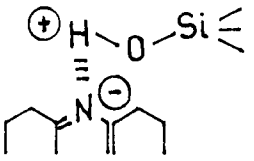
RESULTS AND DISCUSSION

Table I shows the structures of the tested compounds, their k' values in descending order, and their pK values.

Analysis of these data suggested interaction between (a) the C(4)=O groups and the silanol groups of the sorbent, and between (b) the N(1) and silanol groups as the prevailing chromatographic mechanism.



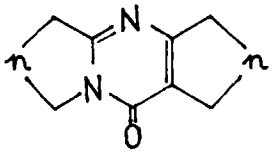
a)



b)

Table 1.

Structure, pK values and chromatographic data of the tested compounds.



Number	Structure			K'	pK
	A	B	C		
1	5	6	5	34,66	2,24
2	5	6	6	27,27	3,18
3	5	6	8	24,69	3,23
4	5	6	7	21,21	3,20
5	6	6	5	19,00	3,46
6	6	6	5 (6 Me)	17,27	3,63
7	6	6	6	13,24	4,47
8	6	6	5 (7 Me)	12,72	3,51
9	6x	6	5 (8 Me)	12,38	
10	6x	6	5	10,72	3,27
11	6	6	8	10,03	4,31
12	6	6	7	9,62	4,42
13	6	6	6 (6 Me)	9,48	4,58
14	8	6	6	9,27	4,09
15	6	6	6x(7 Me)	9,08	4,36
16	5	6	6x	9,00	2,59
16a	6	6	5 (9 Me)	8,76	
17	6x	6	5 (6 Me)	7,50	4,09
18	6x	6	6 (7 Me)	6,48	4,14
19	7	6	8x	5,45	3,99
20	6	6	6x	4,90	3,69
21	8	6	6x	3,41	3,45

x Rings with aromatic character.

The strengths of these bonds may be influenced by the (aromatic) mesomeric effect of ring B, the steric screening effect of rings A and C, and the screening and mesomeric effects of certain substituents.

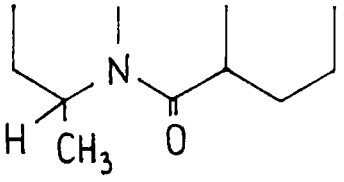
The screening effect increases with increasing size of ring C in 1-7.

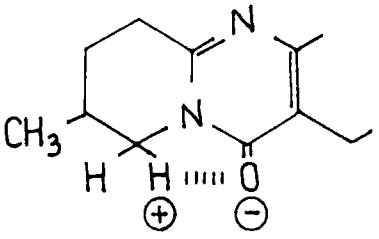
The retention data and pK values indicate, that, as far as the adsorption strength is concerned, this steric effect inactivates mainly the C(4)=O group. For 1-4, the k' values decrease, while the pK values increase. The same sharp contrast can be seen between the k' and pK values of 1 and 7.

The increase in size of ring A from five to six atoms causes stronger steric hindrance (see the k' values of 1 and 2, and of 1 and 5).

The mesomeric effect of ring A, and much more so that of ring C, decreases the retention (see the k' values of 15 and 18, and of 7 and 20).

The blocking effect on CH_3-substitution at position C(6) does not seem significant in all cases 5 and 6 but is much clear of ring C is not five but six-membered (see the k' values of 7 and 13). The CH_3-substitution at position C(7) and C(8) seem more significant reflecting the decreased k' values. This phenomenon may be explained by supposing an interaction between C(6)-H and C(4)=O (see the k' values for 5, 8 and 9), limiting the activity of C(4)=O towards the silanol groups.





The k' values of 10 and 17 reveal that here the adsorption is influenced by the hyperconjugation as well as the steric effect.

REFERENCES

1. Hankó-Novák K. et al.: Acta Pharm. Hung. 51. 246 (1981)
2. Hankó-Novák K. et al.: Acta Pharm. Hung. 53. 17 (1983)
3. Halász-Ignáth Zs. et al.: Acta Pharm. Hung. 53. 203 (1983)
4. Papp O. et al.: J. Chromatogr. 252. 67 (1982)
5. Shalaby A. et al.: J. Liquid Chromatogr. 7. 1133 (1984)
6. Shalaby A. et al.: Proc. of the Symp. on Advences in Liquid Chromatogr. Szeged, Hungary (1982) (Publishing House of the Hungarian Academy of Sciences)
7. Ayyangar, W.R., Srinivasan, K.V.: J. Chromatogr. 267. 399 (1983)
8. Hermecz I. et al.: J. Heterocylic Chem. 20. 93 (1983)
9. Pharmacopeia Hung. VI. I. 299 Medicina Könyvkiadó, Budapest, 1967