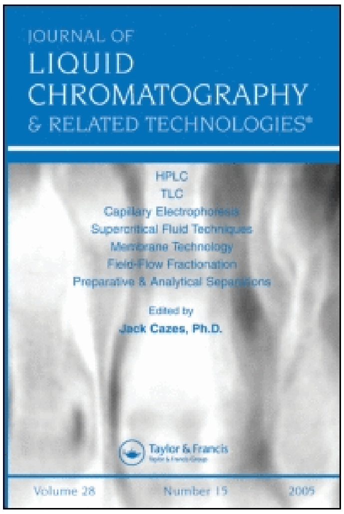

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Ion-Pair Chromatography of Nitrogen-Bridged Compounds on Silica Gel

A. Shalaby[a]; Zs. Budvári-Bárány[a]; Gy. Szász[a]
[a] Institute of Pharmaceutical Chemistry Semmelweis Medical University, Budapest, Hungary

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ION-PAIR CHROMATOGRAPHY OF NITROGEN-BRIDGED COMPOUNDS ON SILICA GEL

A. Shalaby, Zs. Budvári-Bárány, and Gy. Szász
Institute of Pharmaceutical Chemistry
Semmelweis Medical University
Budapest, Hungary

ABSTRACT

New adsorption operations of high-performance ion--pair chromatography have been investigated, using certain types of pharmacologically active nitrogen-bridged compounds. Various chromatographic data are reported. The effect of the counter ion concentration has been studied. Numerous examples of separations are presented.

INTRODUCTION

Reversed-phase ion-pair chromatography is a techniques often applied in HPLC. A recently developed HPLC method is normal-phase ion-pair chromatography /1,2/.

In the present work a new type of dynamic ion-complex system, and ion-pairing system has been developed. In this

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system silica gel is used as stationary phase, together with a mixture of chloroform-methanol containing different concentrations of camphor sulphonic acid (CSA). The results show that, depending on the CSA counter ion concentration, ion-pairing or molecular complexing takes place.

EXPERIMENTAL

Materials

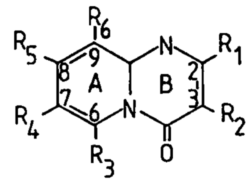
All the model substances were synthetized in our laboratory (see Tables 1-4) /3,4/. Their identification and quality control were performed via melting point determination and chromatography.

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

Chromatography

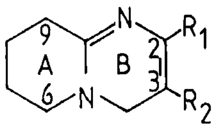
The HPLC apparatus was a LIQUOCHROM Model 2010 (Labor Mim, Budapest, Hungary). A variable-wavelength detector was used, and the column effluent was monitored at different wavelengths between 270 and 330 nm. The Zorbax SIL column measured 250 x 4,6 mm and was prepacked with material with a particle size of 5 μm (DuPont). 20 μl of sample solution (o.1 mg/ml in methanol) was injected. Mobile phase: chloroform-methanol 95:5, with and without different concentration of CSA. The flow rate was 0.7 ml/min. All experiments were run at 25 ^{o}C.

Table 1
STRUCTURE OF MODEL SUBSTANCE



Number of compd.	C_2	C_3	C_6	C_7	C_8	C_9
1	H	H	H	H	H	H
2	CH_3	H	H	H	H	H
3	H	CH_3	H	H	H	H
4	H	H	CH_3	H	H	H
5	H	H	H	CH_3	H	H
6	H	H	H	H	CH_3	H
7	H	H	H	H	H	CH_3
8	CH_3	CH_3	H	H	H	H
9	CH_3	H	CH_3	H	H	H
10	CH_3	H	H	H	H	CH_3
11	H	CH_3	CH_3	H	H	H
12	CH_3	H	C_2H_5	H	H	H
13	C_2H_5	H	CH_3	H	H	H
14	H	C_2H_5	CH_3	H	H	H
15	CH_3	C_2H_5	CH_3	H	H	H
16	CH_3	C_2H_5	CH_3	H	CH_3	H
17	CH_3	C_3H_7	H	H	H	H
18	CH_3	C_3H_7	CH_3	H	H	H
19	C_2H_5	CH_3	CH_3	H	H	H
20	C_3H_7	C_2H_5	CH_3	H	H	H

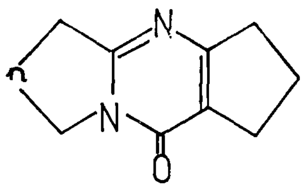
Table.2
STRUCTURE OF MODEL SUBSTANCES



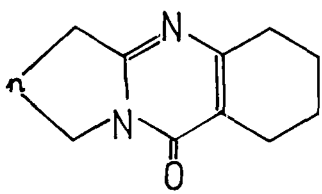
Number of compd.	C_2	C_3	C_6	C_9
21	H	H	H	H
22	CH_3	H	H	H
23	H	CH_3	H	H
24	H	H	CH_3	H
25	CH_3	CH_3	H	H
26	CH_3	H	CH_3	H
27	CH_3	H	H	CH_3
28	H	CH_3	CH_3	H
29	CH_3	C_2H_5	CH_3	H

Table.3
Structure of model substances

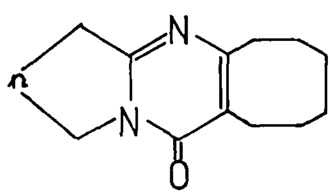
Number of compound	
30.	n = 1
31.	n = 2
32.	n = 3
33.	n = 4
31.a	C_6 Me
31.b	C_7 Me
31.c	C_8 Me
31.d	C_9 Me



34.	n = 1
35.	n = 2
36.	n = 3
37.	n = 4
34.a	C_6 Me
35.a	C_6 Me
35.b	C_7 Me
35.c	C_8 Me
35.d	C_9 Me



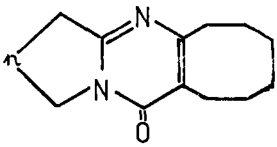
38.	n = 1
39.	n = 2
40.	n = 3
41.	n = 4



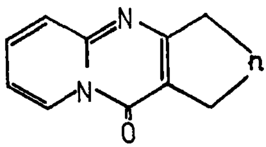
(continued)

Table 3 (continued)

Number of compound	
42.	n = 1
43.	n = 2
44.	n = 3
45.	n = 4



46.	n = 1
47.	n = 2
48.	n = 3
49.	n = 4
46.a	C_6 Me
46.b	C_7 Me
46.c	C_8 Me
46.d	C_9 Me
47.a	C_6 Me
47.b	C_7 Me
47.c	C_8 Me
47.d	C_9 Me



50.	n = 1
51.	n = 2
52.	n = 3
53.	n = 4
50.a	C_6 Me
50.b	C_{12}Me
52.a	C_{12}Me

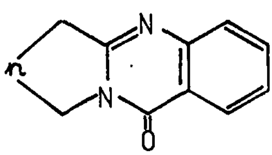
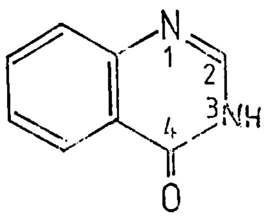


Table.4
Structure of model substances

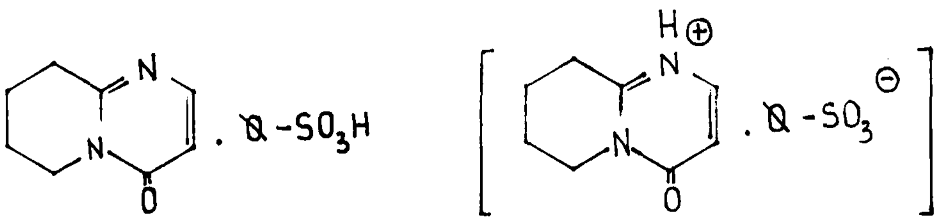


number of compd.	C_2	N_3
54.	H	H
55.	CH_3	H
56.	H	CH_3
57.	CH_3	CH_3
58.	CH_3	C_2H_5
59.	CH_3	C_3H_7
60.	CH_3	C_4H_9
61.	C_2H_5	CH_3
62.	C_2H_5	C_2H_5
63.	C_2H_5	C_3H_7
64.	C_2H_5	C_4H_9

RESULTS AND DISCUSSION

Table 5 shows that the k' values are very small for all the tested compounds in the absence of CSA.

Figure 1 reveals a maximum as a function of the amount of CSA. We suggest that molecular complexation between CSA and the tested compounds is responsible for the increase in the retention time; and ion-pairing process is than responsible for the decrease in the retention time. This may be explained in that in the presences of a small amount of CSA the molecular complex A will form; when the amount of CSA is increased, form B, involving the formation of an ion-pair, can also exist. Consequently, the k' values will decrease.



A B

Table 6 shows the R_s values for some pairs of compounds before and after addition of CSA. Table 5 lists the N and H values calculated with and without application of the counter-ion; these prove that the use of CSA increases

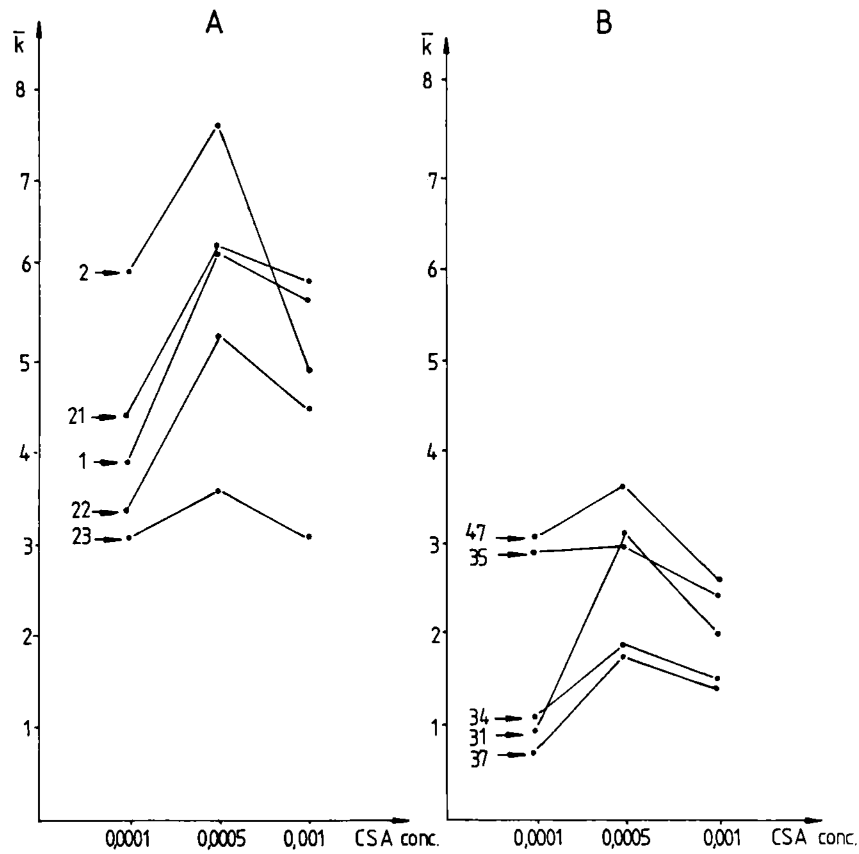


FIGURE 1. Relationship between k' Values and Concentration of CSA.
A - Two Ring System B - Three Ring System

Table 5

Chromatographic data of the tested compounds

Number of compounds	Chloroform-methanol 95:5			Chloroform-methanol 95:5 + 0.001 N CSA		
	$\overline{K}$	N	H	$\overline{K}$	N	H
1	0.4	610	0.409	5.73	4613	0.054
2	0.466	670	0.373	4.83	3462	0.072
3	0.4	610	0.409	5.06	2867	0.087
4	0.4	610	0.409	3.1	3352	0.075
5	0.4	610	0.409	4.6	2443	0.102
6	0.433	640	0.390	4.6	2501	0.099
7	0.2	554	0.451	5.8	2874	0.087
8	0.333	554	0.451	2.83	2930	0.085
9	0.3	650	0.385	7.00	3191	0.078
10	0.133	711	0.352	7.00	2637	0.095
21	0.566	764	0.327	5.86	3673	0.068
22	0.533	732	0.342	4.56	2414	0.104
23	0.5	701	0.356	3.133	5323	0.046
24	0.466	670	0.373	4.93	3582	0.069

25	0.4	610	0.409	4.06	2612	0.096
26	0.4	754	0.332	3.93	3370	0.074
27	0.333	554	0.451	3.266	2521	0.099
30	0.666	670	0.373	4.66	4447	0.056
31	0.4	1085	0.230	2.0	3663	0.068
34	0.533	904	0.277	2.96	3138	0.079
35	0.266	617	0.405	2.43	2350	0.106
35a	0.366	718	0.348	3.26	3630	0.069
35b	0.166	754	0.331	2.43	2350	0.106
35c	0.133	711	0.351	1.05	2328	0.107
35d	0.166	662	0.378	3.066	5153	0.049
36	0.133	1111	0.225	1.5	2543	0.098
37	0.166	424	0.589	1.45	3325	0.075
39	0.2	797	0.314	3.73	4468	0.056
43	0.2	448	0.558	3.00	4986	0.050
47	0.2	797	0.313	2.58	4001	0.062
47a	0.166	754	0.332	3.9	2443	0.102
47b	0.133	711	0.351	2.0	1794	0.139
47c	0.2	797	0.314	2.0	2804	0.089
47d	0.066	630	0.694	5.4	4167	0.059
51	0.2	915	0.273	2.66	4189	0.059
54	1.53	1999	0.125	1.93	4766	0.052
55	1.066	1330	0.188	3.83	4659	0.054
56	0.433	640	0.391	1.166	2600	0.096
59	0.133	711	0.351	2.4	2305	0.108
64	0.00	554	0.451	0.7	3890	0.064

Table 6

The resolution and selectivity factors of some pairs of tested compounds

Number of pairs	Chloroform-methanol 95:5		Chloroform-methanol 95:5 0.001 M CSA	
	R_s	Selectivity	R_s	Selectivity
1 (4+24)	0.25	0.858	4.58	0.628
2 (10+27)	0.85	0.399	6.58	0.466
3 (5+25)	0.00	1.00	1.06	0.883
4 (1+8)	0.25	0.832	7.25	0.494
5 (7+8)	0.53	0.600	6.4	0.488

6 (1+2)	0.25	0.858	1.93	0.843
7 (56+59)	1.28	0.307	4.6	0.486
8 (55+56)	2.37	0.406	10.00	0.304
9 (35+47)	0.3	0.752	0.5	0.941
10 (30+51)	2.05	0.300	6.0	0.571
11 (35+51)	0.31	0.752	0.777	0.914
12 (30+31)	1.14	0.601	8.42	0.429
13 (34+35)	1.11	0.499	1.6	0.820
14 (30+34)	0.5	0.800	4.6	0.635
15 (36+37)	0.156	0.801	0.230	0.966
16 (35+37)	0.394	0.5	3.68	0.592
17 (34+36)	1.5	0.249	5.176	0.507

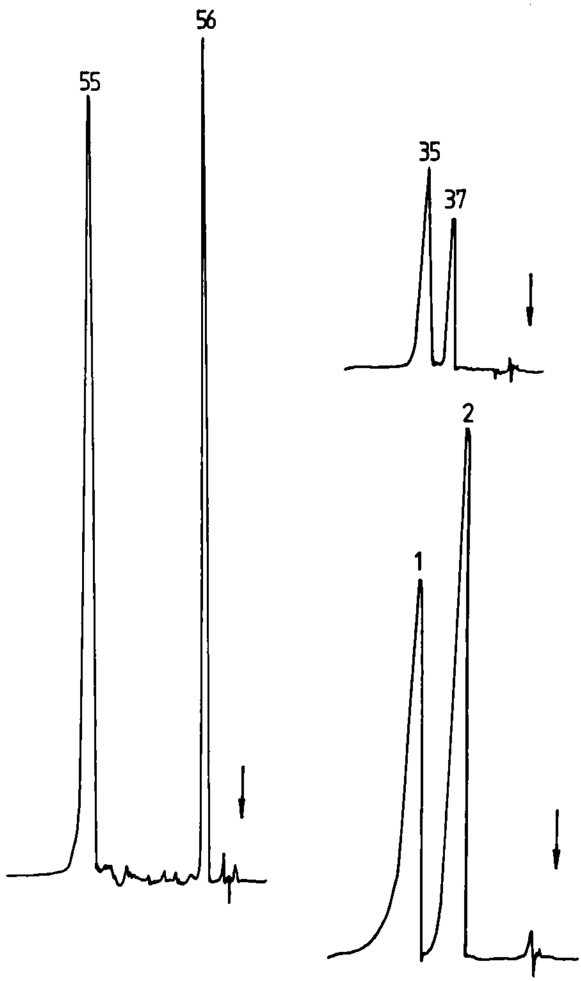


FIGURE 2. Separation of Some Pairs of Compounds by Ion-Pair Chromatography on Silicagel.

Stationary Phase: Zorbax sil., 5 μm

Mobile Phase: Chloroform-Methanol 95:5 + 0,001 M C.S.A.

Flow Rate: 0,7 ml/min

the efficiency of the column and also the selectivity (α). Some chromatograms of structurally closely related compounds are shown in Fig.2.

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