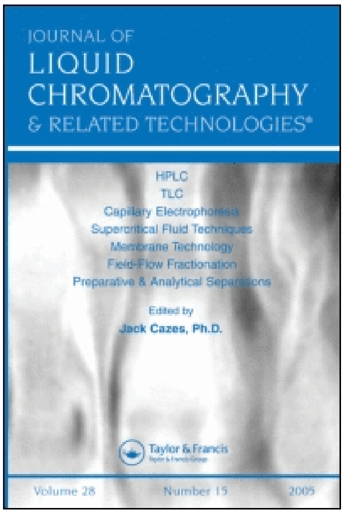

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

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To cite this Article Bao, Fengrong , Wu, Yanying and Wu, Shulin(2000) 'REVERSED PHASE CHROMATOGRAPHY OF SOME HOMOLOGOUS FERROCENOYL AMIDES', Journal of Liquid Chromatography & Related Technologies, 23: 10, 1565 — 1574

To link to this Article: DOI: 10.1081/JLC-100100435

URL: http://dx.doi.org/10.1081/JLC-100100435

J. LIQ. CHROM. & REL. TECHNOL., 23(10), 1565–1574 (2000)

REVERSED PHASE CHROMATOGRAPHY OF SOME HOMOLOGOUS FERROCENOYL AMIDES

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ABSTRACT

Under this research, a reversed phase high performance liquid chromatography (RP-HPLC) separation condition has been found for two series of homologous ferrocenoyl amides: $Fc(CH_2)_m CONH(CH_2)_nH$ (m=1-3, n=4-8) and by reversed phase thin layer chromatography (RP-TLC). The effect of separation for the above two homologous series is satisfactory in the RP-TLC and the RP-HPLC. When "m" was the same and "n" was different, a linear relationship was found between the values of R_M, log K'of the homologs and "n", and between the log K' and the fraction of the organic modifier in the mobile phase (R_M = log (1/R_f - 1) and $F_c = C_5H_5F_eC_5H_4$. When "m" was different but "n" was same, all the first members (m=0) of each group of homologs deviated from a linear relationship between the values of R_M, logK'and "m" of the solute.

INTRODUCTION

Under the leadership of prof. Shi Shu-jian, the Teaching and Research Section of organic chemistry at the Department of Chemistry Inner Mongolia University started researches on the synthesis, properties, and structure of ferrocene derivatives in the 1960's.[1-4] They continued their scientific research of

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ferrocene derivatives in the 1970's, which has enriched the knowledge of ferrocene chemistry.

In the meantime, they also made significant applied research and provided several effective burning rate modifiers of ferrocenes for the production and study of composite solid propellants. But, we peromed little research on the chromatographic behaviour for ferrocene derivatives. In order to determine separation conditions for high performance liquid chromatography for ferrocene derivatives, which involves the regularity between structure and retention values of compounds, we divided ferrocenoyl amide: $Fc(CH_2)_m CONH(CH_2)_nH$ into two homologous series, based on our own original researches,[5-7] and we applied RP-TLC analysis on them with the reversed phase chromatoplates prepared previously by us, then used appropriate developer systems as eluent and carried out RP-HPLC analysis. As a result, not only was the effect of separation for two series of homolog satisfactory, but also the time of needed to select appropriace elution systems for RP-HPLC is diminished, a significant solvent economy is realized, and the expensive chromatographic column is protected.

In order to compare the retention characteristic of the above homologs on the C_8 column, the capacity factor K' values for compounds could be calculated by

$$K' = (t_R - t_O)/t_O \qquad (1)$$

t_R and t_O are the retention time of the solute and a non-retained component, respectively.

EXPERIMENTAL

Reversed Phase Thin-Layer Chromatography

Kieselguhr G was mixed well with 0.6% aqueous solution of carboxymethylcellulose (CMC), then the glass plates (20cm×15cm) were covered with a 0.25mm layer of a slurry of the support with standard equipment, and the plate was dried by air-drying overnight at room temperature and then in an oven at 110°C for about 0.5 hour. Then the plates were placed in a container (developing chamber) with 5% solution of paraffin oil in petroleum ether (30-60°). When the mobile phase migrated to the top of the plate, it was removed and the volatile components of the mobile phase were allowed to evaporate at room temperature in a vented hood. The plates were then place into a desiccator until they were to be used.

After the samples were dissolved in benzene, they was spotted with a capillary tube. Developer, which consisted of mixture of tetrahydrofuran (THF)-acetonitrile-water [0.40:0.12:0.48 (I), by volume] was saturated with paraffin oil. RP-TLC was carried out by the usual ascending procedures. All the spots of components to be separated were yellow; color development was not necessary.

Reversed Phase High Performance Liquid Chromatography

RP-HPLC was carried out at 30°C with a Shimadzu LC-6A system equipped with a SPD-6AV ultraviolet detector (wavelength range 195-700nm, absorbance at 254nm), and LC-6A high pressure pump; chromatographic data were recorded and processed on a C-R3A data system, atten = 8.

The stationary phase was a C_8 column (Shim-Pack CLC-C_8, 5 µm particle size, 150mm × 6mm i.d.). This silica-based packing was fully end-capped to suppress residual silanol group influences.

All samples[4] were synthesized in our own laboratory, to within of 0.5-1.0°C of the melting point and identified by elemental analysis, IR, and NMR spectra. All samples were dissolved in acetonitrile, and an appropriate amount of each sample was injected onto the column according to tits UV detector response.

All the solvents used were analytical grade, redistilled, and filtered by G_6 sand core funnel. Water for solvents were redistilled in a glass distillation system. The mobile phase consisted of a mixture of THF-acetonitrile-water [0.40:0.12:0.48(I), 0.40:0.16:0.44(II), 0.40:0.20:0.40 (III), 0.44:0.12:0.44 (IV), 0.48:0.12:0.40 (V)]. The mobile phase was used after it was degassed by ultrasonic waves. The flow rate of mobile phase was constantly 1.25mL/min.

RESULTS AND DISCUSSON

We divided ferrocenoyl amide $Fc(CH_2)_mCONH(CH_2)_nH$ into four groups of homologs, based on whether m was the same but n was different, their R_M and K' values in reversed chromatography show a regular change; see Table 1.

Table 1 shows that the R_M values of the four groups of homologs increased with the increase of the number n of carbon atom connected to a nitrogen atom, and a linear relationship was shown between R_M values and the number n of carbon atom in RP-TLC; see Figure 1(a).

Table 1

R_g log K' Values of $Fc(CH_2)_mCONH(CH_2)_nH$ and Regression Analysis of the Relationship log K' = log k_w + Sφ

Compounds			Mobile Phase											
	-CH_2-		I	I	II	III	IV	V	Changes of Acetonitrile Conc.			Changes of THF Conc.		
No.	m	n	R_M	log K'	log K'	logK'	log K'	log K'	log K_w	S	r	log K_w	S	r
1	0	4	-0.50	0.021	-0.076	-0.155	-0.092	-0.155	1.162	-2.200	0.9983	1.157	-2.200	0.9868
2	0	5	-0.31	0.140	0.033	-0.056	0.009	-0.066	1.411	-2.450	0.9986	1.470	-2.575	0.9879
3	0	6	-0.18	0.250	0.137	0.041	0.104	0.021	1.606	-2.612	0.9989	1.728	-2.862	0.9876
4	0	7	-0.03	0.358	0.238	0.134	0.199	0.097	1.811	-2.800	0.9991	2.045	-3.262	0.9921
5	0	8	0.07	0.462	0.334	0.225	0.290	0.176	1.999	-2.962	0.9989	2.311	-3.575	0.9932
6	1	4	-0.29	0.155	0.049	-0.041	0.033	-0.051	1.426	-2.450	0.9989	1.488	-2.575	0.9944
7	1	5	-0.12	0.274	0.158	0.057	0.137	0.037	1.682	-2.712	0.9992	1.808	-2.962	0.9960
8	1	6	-0.02	0.387	0.262	0.155	0.233	0.124	1.892	-2.900	0.9990	2.089	-3.287	0.9951
9	1	7	0.14	0.496	0.362	0.248	0.328	0.204	2.105	-3.100	0.9989	2.387	-3.650	0.9962
10	1	9	0.25	0.599	0.459	0.338	0.417	0.281	2.292	-3.262	0.9991	2.658	-3.975	0.9965
11	2	4	-0.18	0.255	0.140	0.037	0.121	0.021	1.670	-2.725	0.9995	1.770	-2.925	0.9965
12	2	5	-0.03	0.369	0.243	0.137	0.220	0.111	1.874	-2.900	0.9987	2.039	-3.225	0.9960
13	2	6	0.09	0.480	0.344	0.228	0.316	0.193	2.115	-3.150	0.9989	2.339	-3.587	0.9966
14	2	7	0.23	0.585	0.442	0.322	0.408	0.272	2.291	-3.287	0.9987	2.613	-3.912	0.9971
15	2	8	0.37	0.686	0.538	0.410	0.496	0.348	2.477	-3.450	0.9991	2.876	-4.225	0.9974
16	3	4	-0.09	0.316	0.196	0.093	0.173	0.072	1.763	-2.787	0.9990	1.895	-3.050	0.9951
17	3	5	0.03	0.430	0.299	0.188	0.272	0.161	2.000	-3.025	0.9989	2.171	-3.362	0.9949
18	3	6	0.16	0.537	0.398	0.279	0.364	0.236	2.211	-3.225	0.9990	2.486	-3.762	0.9963
19	3	7	0.33	0.638	0.493	0.369	0.452	0.314	2.383	-3.362	0.9990	2.736	-4.050	0.9963
20	3	8	0.48	0.738	0.587	0.456	0.538	0.387	2.568	-3.525	0.9992	3.011	-4.387	0.9968

RP-TLC is partition chromatography. In partition chromatography, the components separate according to the difference of their partition coefficients in the stationary phase and mobile phase. The components which prefer the stationary phase are retained longer, having large R_M values and, conversely, those preferring the mobile phase have small R_M values.

FcCONH-, $FcCH_2CONH$-, $Fc(CH_2)_2CONH$- and $Fc(CH_2)_3CONH$- were precursor structures of four groups of homologs, respectively; their contribution to R_f values of homologs were same. The magnitude of R_f values of the above homologs depends on length of the apolar carbon chain $(-CH_2-)_n$ in the molecules, except for common precursors. The increase of the carbon chain, the apolar part, and affinity for the apolar stationary phase, led to an increase of the partition coefficient, a decrease of R_f values, and an increase of R_M value. Thus, the four groups of homologs all show a changing regularity of $R_M(CH_2)_4<R_M(CH_2)_5<R_M(CH_2)_6<R_M(CH_2)_7<R_M(CH_2)_8$.

In RP-HPLC, when mobile phase I, II, III, IV, and V were used to elute, retention times of the four groups of homologs on the C_8 column showed the regularity of $t_R(CH_2)_4<t_R(CH_2)_5<t_R(CH_2)_6<t_R(CH_2)_7<t_R(CH_2)_8$, which means that the retention values (log K') of homologs increased with the increase of n; see Table 1. A linear relationship was shown to exist between log K' values and n; see Figure 1(a'), and the correlation coefficient r = 0.9990-0.9998, can be seen in Table 2. In Table 2, A in the linear equation is the intercept, and the slope B is the sensitivity to carbon number n. The data are listed in Table 2, where it can be seen that the slope B values decreased with the increase of the content of organic modifier (I<II<III, I<IV<V) in the mobile phase, which means a decrease of the contribution of each $(-CH_2-)$ to solute retention.

Based on the observation that m is diffirent but n is same, we can also divide $Fc(CH_2)_mCONH(CH_2)_nH$ into five groups of homologs:1, 6, 11, 16; 2, 7, 12, 17; 3, 8, 13, 18; 4, 9, 14, 19; 5, 10, 15, 20.(see Table 1). The common precursors of the five groups of homologs are $-NH(CH_2)_4H$, $-NH(CH_2)_5H$, $-NH(CH_2)_6H$, $-NH(CH_2)_7$ and $-NH(CH_2)_8$, respectively. The data shown in Table 1 indicates that, under the same chromatographic condition, if the molecular acyl part $Fc(CH_2)_mCO$- has a long chain, the values of R_M are great, and so were the values of log K', which shows consistently changing regularity of $R_M(CH_2)_0<R_M(CH_2)<R_M(CH_2)_2<R_M(CH_2)_3$ and log K' $(CH_2)_0<$ log K' $(CH_2)_1<$ log K' $(CH_2)_2$ < log K' $(CH_2)_3$. But, the examples shown in Figure 1 (b) and (b') indicate that all the first members (m = 0) of the five groups of homologs deviated from a linear relationship between R_M, logK', and m.

The differences of reversed phase chromatographic behaviour of two series of homologs could be explained by the following expression[8]:

Table 2

Sensitivity of Capacity Factor to Chain Length*

Compounds			Mobile Phase														
			I			II			III			IV			V		
No.	m	n	B	A	r	B	A	r	B	A	r	B	A	r	B	A	r
1,2,3,4,5	0	4,5,6,7,8	0.1103	-0.416	0.9998	0.1023	-0.483	0.9998	0.0950	-0.532	0.9998	0.0959	-0.474	0.9999	0.0826	-0.484	0.9998
6,7,8,9,10	1	4.5,6,7,8	0.1108	-0.283	0.9997	0.1024	-0.357	0.9998	0.0947	-0.418	0.9999	0.0953	-0.341	0.9998	0.0838	-0.382	0.9994
11,12,13, 14,15	2	4,5,6,7,8	0.1075	-0.171	0.9997	0.1001	-0.260	0.9998	0.0929	-0.331	0.9998	0.0940	-0.251	0.9997	0.0817	-0.301	0.9994
16,17,18, 19,20	3	4,5,6,7,8	0.1049	-0.098	0.9996	0.0974	-0.190	0.9998	0.0905	-0.266	0.9999	0.0913	-0.187	0.9996	0.0789	-0.241	0.9990

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* $\log K' = A + Bn$

$$\log K' = A' + B'\frac{1-\lambda}{2\lambda} \bullet \frac{\mu_s^2}{V_s} \bullet \frac{1}{1-\frac{\alpha_s}{V_s}} + C'\Delta A \tag{2}$$

where A', B', and C' are constants, λ proportionality factor, V_s molecular volume of the solute, polarizability of the solute, dipole moment of the solute, contact surface area of the associated species. The expression (2) shows that the values of log K' of solute decreased with an increase of the molecular the dipole moment μ_σ, and increased with an increase of the contact surface area of the associated species. The molecular polarities are similar, the dipole moment is in proximity to constant, indicating to the genuine homologous series, the expression above could be simplified to:

$$\log K' = A'' + C'\Delta A \tag{3}$$

where expression (3) indicates that log K' of the homolog and showed a linear relationship, while ΔA was proportional to the hydrocarbonaceous surface area of homologs studied, the number of carbon atoms was proportional to the molecular surface area in the homologs; thus, the relationship between their log K' values and the number of carbon atoms was linear. As a result, in fact, the expressed meaning in expression (3) and the results of Table 2 were entirely equivalent. The four groups of homologs of the first series belongs to the simple case of an increase of only carbon number, so the relationship between log K' values and n obeys the linear equation. But, in the case of the five groups of homologs of the second series, the result is different; only the component of m≠0 in the molecular acyl part $Fc(CH_2)_mCO$- of the compound constituted the genuine homolog; however, if the component m is equal to zero, meaning the carbonyl and ferrocenyl are joined directly, this brings about a conjugative effect and produces an increase of the molecular polarity and the dipole moment, both of which lead to the decrease of the retention values of the compounds.

When a methylene $-CH_2-$ was inserted between the carbonyl and ferrocenyl, the conjugative situation mentioned above is broken, caused the decrease of the molecular polarity and decrease of the diploe moment. In the meantime, their ΔA's increased, the combined influence of these two factors led to an incremental increase in the range of the retention values of the component m=1, so there is greater difference between the retention values of the two components m=0 and m=1. This means $\log K' (CH_2) - \log K' (CH_2)_0 > \log K' (CH_2)_2 - \log K' (CH_2) \approx \log K' (CH_2)_3 - \log K' (CH_2)_2$; the result is that the log K'of component m=0 deviates from a straight line to the lower levels. The results depicted in Figure 1 (b) further indicate that the molecular polarity is great when the acyl in the component is FcCO-(m=0).

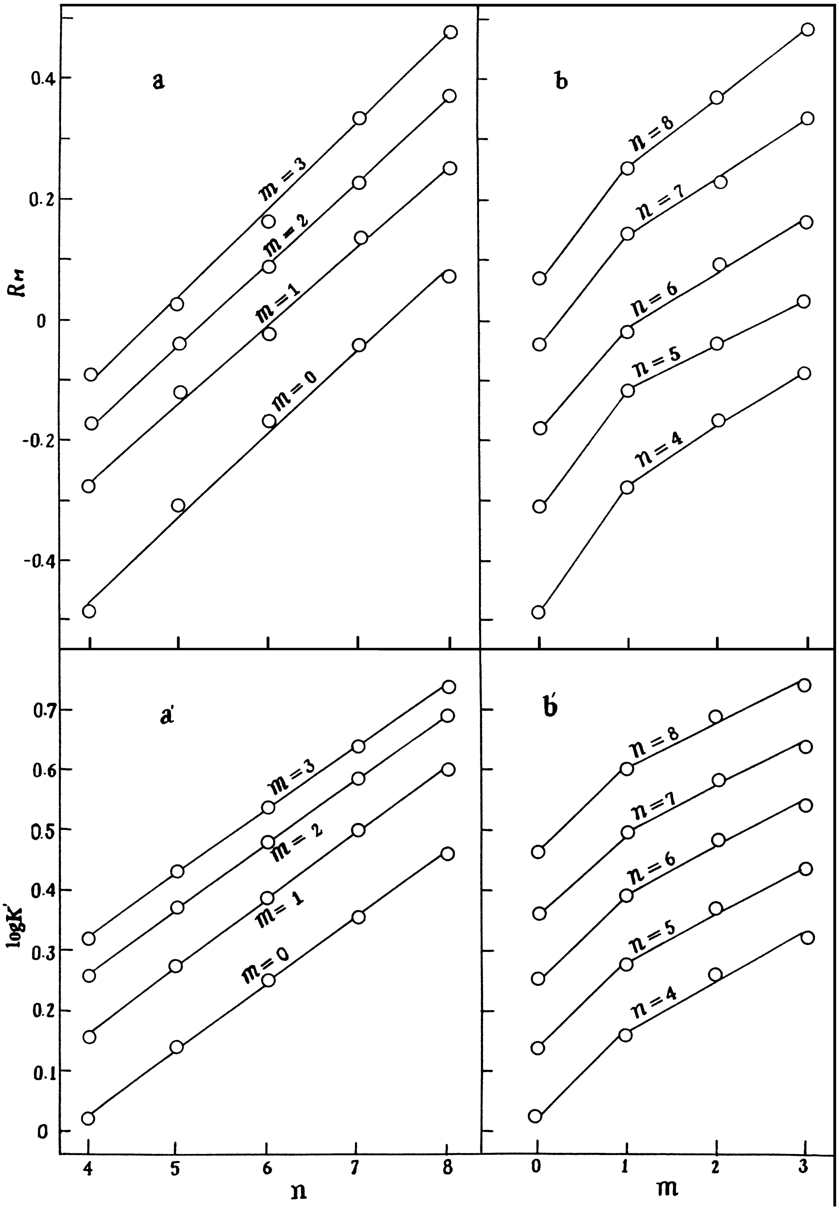

Figure 1. Plots of R_M, log K' vs. number of methylene groups for the ferrocenoyl amide $(Fe(CH_2)_mCONH(CH_2)_nH)$, mobile phase I.

When the content of organic modifier, THF, in the mobile phase is kept unchanged, the values of log K’ of twenty ferrocenoyl amides decreased with the increase of the content(I < II < III) of the acetonitrile, which presents the regularity of log K’(I) > log K’(II) > log K’(III). When the content of the acetonitrile is kept unchanged, the values of log K’ decreased with an increase of the content of the THF (I < IV < V), which presents the regularity of log K’(I) > log K’(IV) > log K’(V) and a linear relationship appeared between the retention value (log K’) and the volume fraction of the organic modifier (acetonitrile, THF) in the mobile phase as shown below:

$$\log K' = \log K_w + S\varphi \tag{4}$$

where φ is the volume fraction of organic solvent in the water-organic solvent mixture, log K_w is the value of log K’ of a solute with pure water as mobile phase (usually obtained by extrapolation to the intercept of the ordinate) and S, the slope of the regression curve, should be related to the solvent strength of the pure organic solvent. If the acetonitrile concentration changes, the values of log K_w vary between 1.162 (1) and 2.568 (20), the values of S between -2.2(1) and –3.525(20), and the values of r between 0.9983 and 0.9995; If the THF concentration changes, the values of log K_w change to between 1.157(1) and 3.011(20), the values of S between –2.2(1) and –4.387(20), and the values of r between 0.9868 and 0.9974. The changing regularity above indicates that, in the range measured, the factors controlling the retention mechanism of compounds were consistent and constant, the negative slope shows that this factor was due to hydrophobic expulsion of the ferrocenoyl amides. As seen in Table 1, the values of log K_w of every group of homologs increased with the increment of the length of an apolar carbon chain of molecule, indicating that log K_w is a better measure of the hydrophobicities of the solutes.

ACKNOWLEDGMENT

This work was supported by the Inner Mongolia Natural Science Foundation of China.

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Received May 10, 1999
Accepted July 19, 1999
Author's Revisions January 15, 2000
Manuscript 5070