CHEMISTRY LETTERS, pp. 951-954, 1976. Published by the Chemical Society of Japan

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY OF COBALT(III) MIXED LIGAND COMPLEXES WITH ACETYLACETONATE AND OXINATE AND MONOMETHYLOXINATE IONS

Yoshinori KIDANI, Shinobu NAGA,* and Hisashi KOIKE*
Faculty of Pharmaceutical Sciences, Nagoya City University, 1-3 Tanabe-dori,
Mizuho-ku, Nagoya 467
*School of Medical Technology and Nursing, Fujita Gakuen University,
Kutsukake-cho, Toyoake-shi, Aichi Prefecture 470-11

In the presence of Co(III) mixed ligand complexes with acetylacetonate, and oxinate and monomethyloxinate ions, the authors attempted to employ high performance liquid chromatography, HPLC, for the separation and purification of the mixed ligand complexes and the reverse phase mode was found to be appropriate. Optimal reaction conditions of the synthesis have been studied.

In the syntheses of Co(III) mixed ligand complexes with acetylacetonate (acac), and oxinate or monomethyloxinate ions,1) the authors employed either alumina or silicate column chromatography for separation. It took a long period of time such as 2 to 4 weeks for the separation and purification. Since it was disadvantageous that the mixed ligand complexes synthesized might be decomposed in the process of the chromatography, the authors attempted to employ HPLC2) in the rapid separation and purification of mixed ligand complexes.

Separation of the Mixed Ligand Complexes   The authors tried separation of $Co(acac)_3$, [A],3a) $Co(acac)_2(oxinate)$, [B],3b) $Co(acac)(oxinate)_2$, [C],3b) and $Co(oxinate)_3$, [D], using Zorbax Sil,2a) eluted with chloroform. Though each complex was recorded as a sharp peak, the two peaks of the expected complexes, B and C, had not been separated completely by means of the liquid-solid phase mode. Then Permaphase ODS2b) of the reverse phase was employed. Elution with a 10% methanol solution showed broadening of D peak, while all of the complexes were eluted within 5 min with a 30% methanol solution, and the separation of each complex was unsuccessful. Here, the authors employed the linear gradient method of the water-methanol system, in which methanol was added to water in 2% every minute. Fig. 1 illustrates the chromatogram, in which complete separation of the mixed ligand complexes, B and C, was observed as sharp peaks respectively. According to the similar conditions, Co(III) mixed ligand complexes containing acac and monomethyloxinate ions showed complete separation.

The retention time, t_R, and the relative retention time, $t_R/t_{R'}$, to naphthalene as an internal standard are tabulated in Table I. Each mixed ligand complex has been separated well under the conditions employed and this method may be applicable to the identification of the mixed ligand complexes in the synthesis. The degree of separation, R, from the adjacent peaks are shown in Table II. The lowest R value was 1.5, while the highest one 6.5, indicating satisfactory separation.

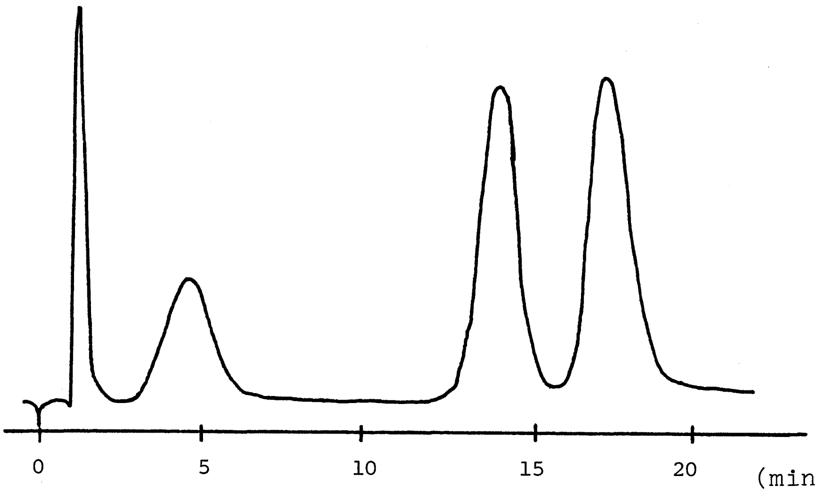

Fig. 1 Chromatogram of Co(III) mixed ligand complexes with oxinate and acetylacetonate ions.

Table I Retention times of Co(III) mixed ligand complexes and their parent complexes

L^*	$Co(acac)_2(L)$		$Co(acac)(L)_2$		$Co(L)_3$	
	t_R(min)	$t_R/t_{R'}$**	t_R(min)	$t_R/t_{R'}$	t_R(min)	$t_R/t_{R'}$
oxinate	4.6	0.21	13.2	0.61	17.4	0.80
2-Me-oxinate	8.5	0.39	18.7	0.86	28.7	1.32
4-Me-oxinate	7.6	0.35	21.0	0.96	26.2	1.20
5-Me-oxinate	8.1	0.37	21.6	0.99	26.5	1.22
7-Me-oxinate	6.4	0.29	19.0	0.87	26.0	1.19

*Me denotes methyl group. **$t_R/t_{R'}$ (relative retention time) was calculated with retention time of naphthalene(t_R=21.8 min) which was used as an internal standard.

Selection of the Synthetic Conditions The authors examined synthetic conditions by means of the HPLC method. In the reaction between 50 ml of 0.1 M A methanol solution and 50 ml of 0.1 M oxine methanol solution, the reaction mixture was refluxed, (1) for 7 min in the presence of 500 mg of active charcoal, and (2) for 180 min without charcoal. In the presence of active charcoal, four peaks of t_R= 2, 5, 13, and 18 min had been observed and they corresponded to those of A, B, C, and D complexes. On the other hand, no peaks corresponding to the mixed ligand complexes were recognized without charcoal. Instead of methanol, less polar solvents such as chloroform and benzene were used and the mixture was refluxed for 180 min in the presence of active charcoal, but no peaks of mixed ligand complexes had been observed by means of HPLC.

In the place of active charcoal, 500 mg each of active kieselguhr, talc, cellulose powder, silica-gel, and active alumina were examined respectively in methanol solution under the similar conditions of refluxing 180 min, but none of the catalysts indicated formation of mixed ligand complexes.

In the synthesis of Co(III) mixed ligand complexes with acac and oxinate ions, active charcoal was found to be indispensable, and such a polar solvent as methanol is recommended to the synthesis, rather than chloroform and benzene.

Fig. 2 shows the change of the species in the reaction solution. Under the conditions examined above by HPLC, synthesis was proceeded and each peak of the components in the reaction solution was determined every minute by HPLC from the calibration curves and the amount was plotted against time as percentile.

Table II Degree of separation from the adjacent peaks

Complexes \ L	oxinate	2-Me-oxinate	4-Me-oxinate	5-Me-oxinate	7-Me-oxinate
Co(acac)$_3$					
	1.9	4.7	3.3	3.8	3.6
Co(acac)$_2$(L)					
	4.1	4.9	5.4	5.6	6.5
Co(acac)(L)$_2$					
	1.5	5.9	2.1	1.9	3.5
Co(acac)$_3$					

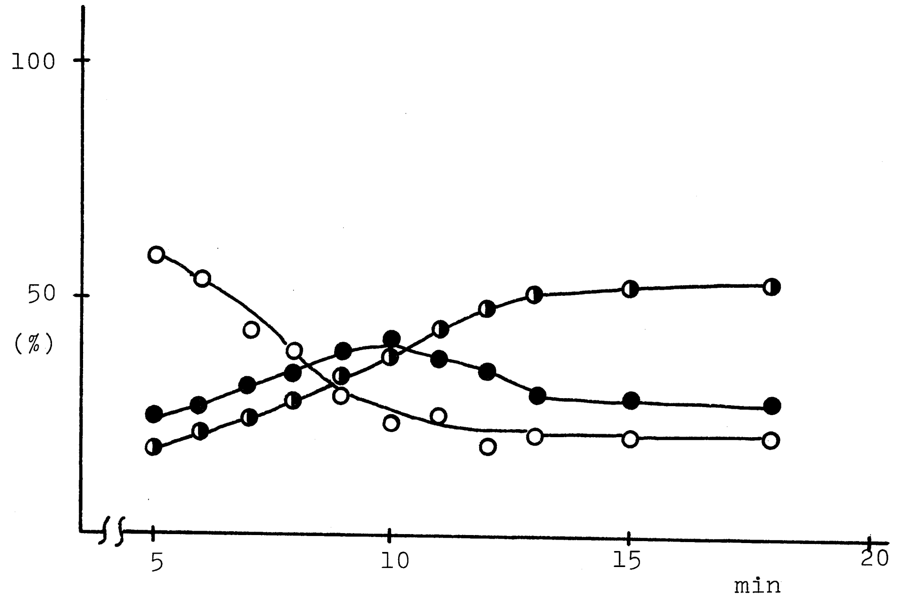

Fig. 2 Change of species in a reaction solution with time

○——○ Co(oxinate)$_3$ D

●——● Co(acac)(oxinate)$_2$ C

◐——◐ Co(acac)$_2$(oxinate) B

After 5 min, about 60% of D was produced and 20 ~ 30% of B and C, the mixed ligand complexes, were synthesized. Gradually B and C were dominating, while D was decreased. Both B and C were about the same amount after 10 min. However, after 15 min, more than 50% of B was produced, while C was decreased and D became less than 20%. This indicates that initially D is synthesized abundantly after 5 min, and then mixed ligand complexes are produced. The authors attempted the reverse reaction by reacting acac with D and formation of mixed ligand complexes, B and C, were recognized by HPLC and TLC.

High performance liquid chromatography is recommended as a simple and effective tool in the separation and purification of the mixed ligand complexes, as well as the selection of the optimal synthetic conditions.

More detailed studies on solvents, amount of catalysts, reaction period of time and reaction temperature are in advance.

Reference and Notes

1) Y. Kidani, S. Naga, and H. Koike, Bull. Chem. Soc. Japan, 48,1436 (1975).
2) A Shimazu-Du pont 830 liquid chromatograph was used with a) Zorbax Sil (2.1 x 250 mm) in the liquid-solid adsorption chromatographic mode, and b) Permaphase ODS (2.1 x 1000 mm) in the reverse phase.
3a) Tris(acetylacetonato)cobalt(III) was purchased from Tokyo Kasei Co., Ltd. and was recrystallized from water once.
3b) Samples of Co(III) mixed ligand complexes were synthesized in our laboratory.

(Received July 12, 1976)