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HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY OF HOMOLOGOUS TITANAINDENE COMPLEXES

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SUMMARY

The high-performance liquid chromatographic (HPLC) behavior of homologous titanaindene complexes has been investigated. Various polar (silica, cyano-bonded, phenyl-bonded) and non-polar (C_{18}-bonded) adsorbents were employed in this study for normal-phase and reversed-phase HPLC, respectively. Data reported include capacity factors (k'), separation efficiencies (N), tailing factors (T) and compound resolutions (R). Normal-phase separation of a titanaindene structural isomer pair on a phenyl-bonded silica column is demonstrated.

INTRODUCTION

Many organometallic compounds are relatively unstable and therefore are not easily separated and analyzed by conventional chemical techniques[1–4]. Gas chromatography (GC) is not useful if the compounds are involatile or thermally unstable[1,3]. Thin-layer chromatography (TLC) and conventional column liquid chromatography (LC), when employable, frequently offer insufficient separating efficiency and tend to be slow[1]. High-performance liquid chromatography (HPLC), in contrast, is a versatile, efficient, relatively rapid separation method for large, non-volatile, thermally labile, air- and water-sensitive compounds. It is thus an ideal technique for the separation and study of many organometallics.

HPLC separation of organometallics was first reported by Veening *et al.*[5–7]. The natural extension of HPLC to metal chelate separations was demonstrated in 1972 by Huber *et al.*[8]. The primary use of HPLC in the separation of cyclopentadienyl-substituted organometallics, an area which has been frequently studied, was first developed in 1973 by Eberhardt *et al.*[9,10]. Since these initial papers, HPLC studies of organometallics have appeared regularly in the literature. Normal-phase and reversed-phase HPLC have been used in the separation of isomeric arene-tricarbonyl-chromium compounds[6], tricarbonyl(dinone)-iron compounds[11], ferrocene and ferrocene analogues[12], psi-*endo* and psi-*exo* dienol-iron-carbonyl isomers[13], *cis*/*trans* isomers of cyclopentadienyl-cobalt-cyclobutadiene[1,12], organomercurials[14], organotin compounds[15], boron, cobalt, sulfur and iron metallocarborane-pi-complex-

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es[2], nonacarbonyl-iron-di-*tert.*-butylsulfurdiimine reaction products and by-products[3], organophosphorus compounds[16], organolead compounds[17], nickel-based organometallics[18], and cyclopentadienyl molybdenum and cobalt cyclobutadienes[4]. We recently reported separation of titanium, zirconium and hafnium metallocene dichlorides[19].

This brief review clearly shows the applicability of HPLC to the separation and study of organometallic compounds, especially for kinetic studies, reaction mechanism determination and preparative purification.

In this study, the results of the chromatographic characterization of homologous titanaindene complexes on various HPLC stationary phases are reported. Both untreated silica and chemically bonded silica phases were examined with a variety of mobile phases. Also reported is the separation of titanaindene structural isomers on a phenyl-bonded silica column in a hexane mobile phase. This separation shows potential use in the purification of titanaindene reaction products and related metallocyclic derivatives.

EXPERIMENTAL

An IBM Instruments (Danbury, CT, U.S.A.) microprocessor-controlled Model LC/9533 ternary gradient liquid chromatograph equipped with an IBM Instruments Model LC/9522 ultraviolet detector was used. The pumping system consisted of an electronically driven three-headed reciprocating piston pump with pistons set 120° apart producing a flow that exhibited only slight variations. The LC/9522 UV detector was a single wavelength unit set at 254 nm with a 10-μl flow-cell volume and a 10-mm pathlength. Prepacked 5.0-μm particle stainless-steel columns (250 mm × 4.5 mm I.D.) were also obtained from IBM Instruments. A Houston Instruments (Austin, TX, U.S.A.) Omniscribe linear chart recorder was used to record all chromatograms. Certified ACS Spectroanalyzed hexane was utilized; all other solvents were HPLC grade. All complexes were dissolved in 0.01 ml of benzene and diluted with 0.40 ml of hexane or acetonitrile for normal-phase or reversed-phase chromatography, respectively. Appropriate amounts were injected to produce 50–60% of the full scale deflection on the 10-mV chart recorder.

Compound 1 [1,1-bis(h^5-cyclopentadienyl)-2,3-di(pentafluorophenyl)benzotitanole][20] was prepared by the thermolysis of diphenyltitanocene[21] and bis(pentafluorophenyl)acetylene[22,23]. The two starting materials were dissolved in anhydrous benzene and refluxed for 1.5 h under argon. An appropriate amount of alumina was added to the resultant solution and the solvent was removed under reduced pressure. The residue was added to a column of alumina and eluted with hexane, hexane–benzene (5:1), hexane–benzene (3:1), and hexane–benzene (1:1) with the first three solvent fractions being discarded. The hexane–benzene (1:1) eluent was brought to a residue under vacuum and the product was recrystallized from diethyl ether–heptane.

Compound 2 [1,1-bis(h^5-cyclopentadienyl)-2,3-di(trifluoromethyl)benzotitanole][20] was prepared by the thermolysis of diphenyltitanocene and hexafluoro-2-butyne (PCR Research Chemicals, Gainesville, FL, U.S.A.). Diphenyltitanocene was dissolved in anhydrous benzene in a Carius tube. An excess of hexafluoro-2-butyne was bled into the tube which was then sealed under liquid nitrogen and refluxed for

4 h. After this period, the contents were transferred to a Schlenk tube, an appropriate amount of Florisil was added and the solvent removed under vacuum. The residue was added to a column of Florisil and eluted with hexane, hexane–benzene (5:1), and hexane–benzene (2:1). Elution with hexane–benzene (1:1) and pure benzene produced the product which was recrystallized from diethyl ether–heptane and dried under vacuum overnight at ambient temperature.

Compounds 3 and 4 [1,1-bis(h^5-cyclopentadienyl)-2-(*p*-tolyl)-3-phenylbenzotitanole and 1,1-bis(h^5-cyclopentadienyl)-2-phenyl-3-(*p*-tolyl)benzotitanole] were prepared[24] by the thermolysis of diphenyltitanocene and *p*-methyldiphenylacetylene in a fashion generally similar to that of compounds 1 and 2; the exact details will be published later.

All chromatograms, unless otherwise noted, were obtained at a flow-rate of 1.0 ml/min and a temperature of 28°C. All solvents were helium degassed prior to use. UV detection was at 254 nm and an attenuation of 0.200 a.u.f.s. was employed. Each chromatogram represents *ca.* 500 ng of total compound injected.

The retention volume (V_R) of each compound was obtained by multiplying the compound retention time (t_R) by the flow-rate. Column void volume (V_0) was determined as the retention volume of the solvent employed, *i.e.* benzene. The capacity factor (k') for the four compounds was calculated from $k' = (V_R - V_0)/V_0$, where V_R is the apparent compound retention volume and V_0 is as defined above. Column efficiency (N) was computed from $N = 5.55\ (t_R/t_w)^2$, where t_R is the compound retention time and t_w is the peak width at half peak height. Resolution (R) of adjacent peaks was obtained by dividing the distance between peak centers by the average peak width; $R = 2\ (t_2 - t_1)/(t_{w1} + t_{w2})$. Finally, tailing factors (T) were determined by drawing a normal line from the peak apex to the baseline and dividing the length of the first half of the peak baseline (x) by the length of the second half (y) and then multiplying the resulting ratio by a factor of 100, *i.e.* $T = 100\ (x/y)$ (100 = perfectly symmetrical peak).

RESULTS AND DISCUSSION

The chromatographic behavior of a group of homologous titanaindenes was investigated on three polar adsorbents (silica, cyano-bonded and phenyl-bonded silica) and a non-polar adsorbent (C_{18}-bonded silica). The organometallics are depicted in Fig. 1. The silica phase was chosen to begin this work since much literature cites silica in the LC separation of such organometallic compounds. The cyano-bonded and phenyl-bonded silica phases, on the other hand, were chosen for the possibility of valuable selectivity effects. Solvent strength in these normal-phase systems was varied from hexane (polarity index (PI(= 0.1) to methylene chloride (PI = 3.1) with intermediate strengths obtained by employing appropriate mixtures of the two. All polarity indices are as listed in ref. 25.

The reversed-phase system (C_{18}-bonded silica) was chosen to investigate any special selectivity afforded by a non-polar column as well as to examine the extent of compound degradation attributable to water exposure. Polar solvent strength was varied by altering the nature and quantity of organic modifiers [acetonitrile (PI = 5.8), methanol (PI = 5.1) or 2-propanol (PI = 3.9)] in an aqueous mobile phase.

TLC on silica was first carried out on the titanaindenes to assess their potential

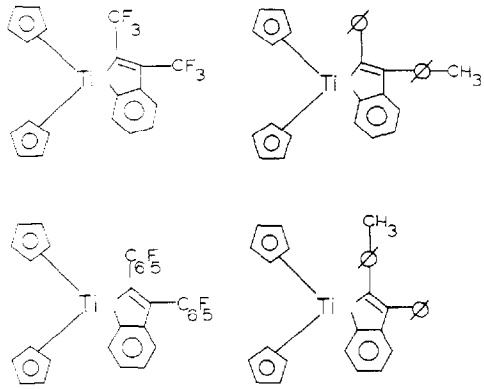

Fig. 1. Structures of the titanaindenes studied. Compounds 2, 1, 3 and 4 (counterclockwise from upper left).

separation by HPLC. Various solvent systems were employed and hexane was chosen as the most desirable. Representative R_F values for two of the compounds studied are listed in Table I.

TABLE I

TLC R_F VALUES FOR TWO TITANAINDENES ON SILICA

	Compound 1	*Compound 2*
Hexane	0.11	0.78
Carbontetrachloride	0.76	0.12
Benzene	0.93	0.53
Methylene chloride	1.00	0.91
Chloroform	0.12	0.60

Fig. 2 shows the results of the HPLC of the titanaindenes on silica with a hexane mobile phase. Although reasonable resolution was obtained between most of the compounds, the isomer pair was not completely separated. Further work on silica revealed that a less polar mobile phase would be necessary to afford any possibility of isomer separation. Increasing the mobile phase polarity decreased all compound retention volumes as well as generally decreasing resolution (especially in the case of the isomers). Chromatographic parameters for the titanaindenes studied are listed in Table II for the optimum chromatography achieved on the silica phase.

Similar results were obtained with the cyano-bonded silica phase. Acceptable resolution was obtained between compounds 1 and 2 but the isomer pair (3 and 4) remained unresolved. Again increasing the solvent polarity gave less effective chromatography. Chromatographic data for the compounds on cyano-bonded silica with a mobile phase of 100% hexane is listed in Table III. Capacity factors for the isomers were not estimated because of the poor resolution encountered.

Much more encouraging results were obtained, however, with the phenyl-bonded phase. As with the other normal-phase systems, increasing solvent polarity

Fig. 2. Chromatogram of titanaindenes on silica with hexane elution.

TABLE II

CHROMATOGRAPHIC PARAMETERS FOR TITANAINDENES ON SILICA WITH HEXANE ELUTION

Compound	V_R *(ml)*	*N*	*k'*	*T*
1	16.2	16,200	3.63	43
2	15.2	14,200	3.34	35
3	7.8	8400	1.23	–
4	9.1	11,500	1.60	–
	$R_{1,2}$ = 0.63			
	$R_{1,3}$ = 4.90			
	$R_{3,4}$ = 0.31			

TABLE III

CHROMATOGRAPHIC PARAMETERS FOR TITANAINDENES ON CYANO-BONDED SILICA WITH HEXANE ELUTION

Compound	V_R *(ml)*	*N*	*k'*	*T*
1	13.9	11,900	3.09	43
2	9.9	13,600	1.91	56
3	7.6	8000	1.24	–
4	7.6	8000	1.24	–
	$R_{1,2}$ = 3.20			
	$R_{1,3}$ = 2.20			
	$R_{3,4}$ = 0.00			

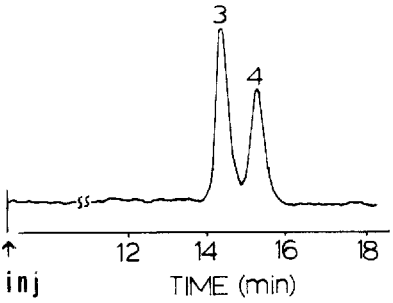

Fig. 3. Titanaindene isomer separation on phenyl-bonded silica with hexane elution.

was detrimental to the chromatography, hence 100% hexane was employed as the mobile phase. In contrast to the results for the silica and cyano-bonded silica columns, the selectivity offered by the phenyl substituents was sufficient to bring about resolution of all compounds including the isomer pair. Apparently the nature of the electronic interaction associated with the compounds and the stationary phase provided the selectivity necessary for separation. Fig. 3 shows the separation of the two titanaindene isomers with 100% hexane on the phenyl-bonded silica phase. Complete chromatographic data for all of the compounds is listed in Table IV. Duplicate trials of the isomer separation run at slower flow-rates *i.e.*, 0.70 ml/min showed improved resolution with little loss in chromatographic efficiency. Resolution of the isomers under these conditions appears to be sufficient to allow successful application of HPLC to the preparative purification of these compounds.

TABLE IV

CHROMATOGRAPHIC PARAMETERS FOR TITANAINDENES ON PHENYL-BONDED SILICA WITH HEXANE ELUTION

Compound	V_R *(ml)*	*N*	*k'*	*T*
1	30.8	25,900	8.18	120
2	14.6	18,900	3.36	75
3	12.0	19,800	2.57	100
4	13.0	17,000	2.72	100
	$R_{1,2}$ = 6.30			
	$R_{1,4}$ = 2.00			
	$R_{3,4}$ = 0.70			

Chromatography of the titanaindenes was also attempted with a reversed-phase system. Using C_{18}-bonded silica as the stationary phase, various experiments were run using a variety of organic modifiers in an aqueous mobile phase. Increasing the water content of the mobile phase typically increased compound retention volumes and caused compound degradation resulting in an increased number and poorer quality of the eluting peaks. Acetonitrile, 2-propanol and methanol were all tried as the organic constituent of the mobile phase. The protic solvents (alcohols) showed

no advantages and contributed to compound degradation when retention volumes were large. Accordingly, acetonitrile was investigated thoroughly especially in the light of studies[26,27] that show that it is the most desirable carrier modifier to bring about significant selectivity changes and optimize separation in reversed-phase HPLC. Despite extensive variation of acetonitrile content in the mobile phase, isomer resolution was not obtainable. Compounds 1 and 2 were, however, easily separated with minimal degradation. Table V lists the chromatographic data for the conditions employed (mobile phase: 85% acetonitrile in water). A single capacity factor is listed for both of the isomers since they were virtually unresolved. Based on the results with this system, reversed-phase HPLC is not applicable to the separation of these organometallic isomers but may be useful for less taxing organometallic separation problems or for less water-sensitive compounds.

TABLE V

CHROMATOGRAPHIC PARAMETERS FOR TITANAINDENES ON C_{18}-BONDED SILICA

Eluent: acetonitrile–water (85:15).

Compound	V_R *(ml)*	*N*	*k'*	*T*
1	5.3	3900	0.46	75
2	9.1	11,500	1.68	100
3	9.0	11,200	1.65	92
4	9.0	11,200	1.65	92
	$R_{1,2}$ = 5.85			
	$R_{1,3}$ = 0.10			
	$R_{3,4}$ = 0.00			

CONCLUSIONS

In normal-phase HPLC, the chromatographic behavior (specifically, retention volume) of the titanaindenes studied seems to be governed by the polarity of the substituents in the ligands. Larger, more fluorinated substituents increase compound retention time while lack of fluorinated substituents causes more rapid elution even for compounds of approximately the same molecular weight (compounds 3 and 4 by comparison with compound 1). The use of a cyano-bonded silica phase does not appear to offer any advantages over unmodified silica based upon these chromatographic results. Phenyl-bonded silica, however, offers sufficient selectivity to resolve all these titanaindenes and therefore shows promise for analytical and preparative HPLC of these compounds.

Reversed-phase HPLC elution of the titanaindenes also showed dependence on the polarity of the ligand substituents. The greater the number of electron-withdrawing groups (F), the more rapid the elution. Very large conjugated electron systems, however, seemed to dictate a certain retention behavior regardless of the number of electron-withdrawing substituents involved (compound 2 by comparison with compounds 3 and 4). Use of different organic modifiers in the aqueous mobile phase did not significantly alter the chromatographic results. Extended exposure to large concentrations of protic solvents (water and alcohols) did cause eventual compound

degradation, however. A mobile phase of acetonitrile–water (85:15) was sufficient to resolve compounds 1 and 2 from the isomer pair (3 and 4) but resolution of the isomer was not achieved in this reversed-phase system. Based on these results, it would appear that reversed-phase HPLC is not applicable to the separation of isomer pairs of this kind and normal-phase HPLC should be employed.

Finally, since mobile phase polarity affected the separation so drastically in the normal-phase systems tried, future work will include the investigation of the effects of use of novel, less polar solvents such as 1,1,2-trichloro-1,2,2-trifluoroethane (PI = 0.0) in the mobile phase.

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