Facile Separations of Enantiomers of Chiral Organometallic Compounds with a Bakerbond Chiralcel HPLC Column

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Summary: Enantiomers of 22 compounds of the formula (η^5-C_5R_5)M(L)(PAr_3)(X) (M/L = Re/NO, Fe/CO) are separated under the title conditions (hexane/2-propanol). In each case, theoretical plate numbers, capacity factors, separation factors, and resolution are determined. Trends in these data and compounds for which enantiomers are not resolved are discussed.

The use of HPLC for preparative and analytical separations of organometallic compounds is well established.[1] However, there has been increasing interest in chiral, optically active organometallic compounds.[2] Recently, many advances have been made in technology for the separation of enantiomeric compounds by HPLC.[3] However, in only a few cases have chiral-HPLC supports been shown to resolve enantiomeric organometallic compounds.[4] In this note, we report that a commercially available HPLC column, Bakerbond Chiralcel OD, is broadly applicable for analytical separations of many enantiomeric "chiral-at-metal" cyclopentadienyl organometallic complexes.

Results

Chromatographic data are summarized in Table I and Chart I. In a typical run, 5–15 μL of an ca. 0.1 M sample was injected and eluted with hexane/2-propanol. Complexes for which enantiomers were separated are shown in Chart I part A. A representative chromatogram is given in Figure 1.

Naturally, enantiomer retention times (t_1 and t_2) were affected by the hexane/2-propanol ratio. Complexes eluted faster with increasing 2-propanol concentrations. In 95:5 hexane/2-propanol, the following order of elution was observed (mean of the two enantiomers of each complex): **19, 11, 13, 20, 18, 1, 16, 8, 22, 9, 7, 6, 15, 12, 14, 5, 2, 10, 3, 4, 21, 17.**

Other data presented in Table I include:[5] theoretical plate numbers (N), a measure of column efficiency; capacity factors k_1' and k_2', which reflect the partitioning of substrate between the mobile and stationary phases; separation factors (α), which are a measure of separation selectivity; resolution (R_s). When $R_s = 1$, only 2% of one band overlaps the other.[5] Larger values indicate better separation. Thus, the Chiralcel OD column gives baseline resolution of the enantiomers of most of the compounds in Chart I part A.

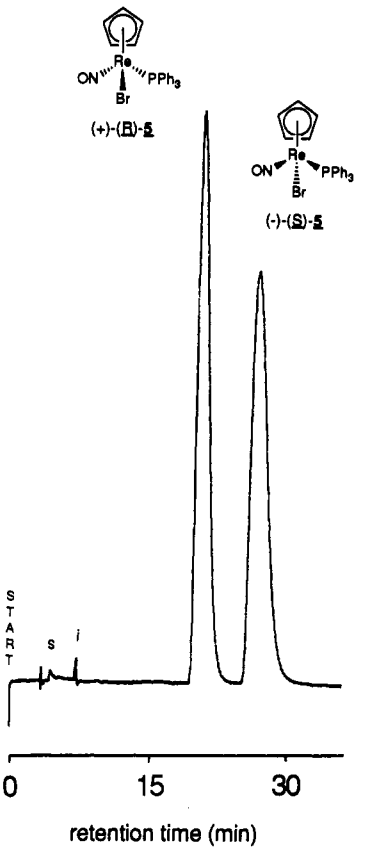

Figure 1. A representative chromatogram. The two peaks intergrate to 50.3:49.7: conditions as per Table I; s = injection solvent; i = impurity.

Complexes **1, 5, 6, 7, 9, 11, 12,** and **15** have been previously prepared in optically active form by routes that allow the absolute configuration at rhenium to be assigned. Thus, authentic samples of (–)-(*R*)-**1**, (+)-(*R*)-**5**, (+)-(*R*)-**6**, (+)-(*S*)-**7**, (+)-(*R*)-**9**, (+)-(*S*)-**11**, (–)-(*S*)-**12**, and (+)-(*S*)-**15** were similarly analyzed by HPLC. These data showed that for **5, 6, 7,** and **9**, the enantiomers with the rhenium configuration (relative) shown in I (Chart I part A) eluted the fastest ((+)-(*R*)-**5**, (+)-(*R*)-**6**, (+)-(*S*)-**7**, (+)-(*R*)-**9**), as illustrated for bromide complex **5** in Figure 1. In contrast, for **1, 11, 12,** and **15**, the enantiomers with the relative configuration opposite to I eluted the fastest ((–)-(*R*)-**1**, (–)-(*R*)-**11**, (+)-(*R*)-**12**, (–)-(*R*)-**15**). Thus, there is not a consistent pattern of chiral recognition with respect to the sterically differentiated PPh_3, cyclopentadienyl, and nitrosyl ligands that remain constant. Hence, the order of elution cannot presently be used to assign configuration to enantiomers in this series of compounds.

Complexes that gave only a single HPLC peak under the above conditions are summarized in Chart I part B. In no case was evidence for two closely spaced maxima, and/or shoulders, observed. However, some peaks were

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Table I. Data on HPLC Separations of Enantiomeric Organometallic Compounds

complex	hexane/2-propanol	flow, mL/min	t_1, min	t_2, min	N^a	$k_1'^b$	k_2'	α^c	R_s^d
1	95:5	0.25	32.78	36.41	5132	1.73	2.03	1.17	1.97
2	98:2	1.0	20.14	22.71	2463	3.47	4.04	1.16	1.65
3	95:5	1.0	26.71	38.30	2075	5.28	8.01	1.52	12.11
4	95:5	1.0	26.78	38.52	2441	5.62	8.52	1.52	9.58
5	95:5	1.0	20.82	27.00	1072	4.20	5.75	1.55	2.05
6	95:5	1.0	13.25	14.78	2213	2.33	2.71	1.16	1.28
7	95:5	0.6	17.79	20.90	2685	2.02	2.55	1.26	2.12
8	95:5	0.5	17.58	20.20	3379	1.12	1.43	1.28	2.00
9	95:5	0.5	20.89	29.39	1938	1.69	2.78	1.65	4.04
10	95:5	1.0	19.30	22.98	1930	3.62	4.50	1.24	1.78
11	95:5	1.0	6.30	7.07	1891	0.62	0.82	1.32	1.27
12	95:5	1.0	17.04	25.70	1415	3.06	5.12	1.67	3.61
13	95:5	1.0	6.72	7.76	1152	1.07	1.39	1.30	1.25
14	95:5	0.5	37.53	40.18	4371	3.49	3.80	1.09	1.12
15	95:5	0.5	31.42	35.35	3124	3.51	4.35	1.24	2.53
16	95:5	1.0	8.73	9.63	1264	0.88	1.07	1.22	0.84
17	90:10	1.0	52.80	58.77	1594	12.42	13.93	1.12	1.59
18	99.5:0.5	1.0	21.94	23.37	2115	2.47	2.69	1.09	0.59
19	95:5	1.0	6.25	7.04	776	0.37	0.54	1.47	0.81
20	95:5	0.5	15.00	17.49	1328	0.76	1.05	1.39	1.46
21	90:10	1.0	32.06	51.92	1298	7.23	12.33	1.71	4.39
22	95:5	1.0	9.03	9.61	3482	1.03	1.17	1.13	0.85

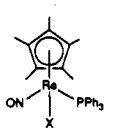
$^a N = 5.54(t_R/t_{w1/2})^2$; t_R = retention time for component R, $t_{w1/2}$ = half height peak width. $^b k_R' = (t_R - t_0)/t_0$; t_0 = column void time. $^c \alpha = k_1'/k_2'$. $^d R_s = (1.18\Delta t_R)/(\sum t_{w1/2})$.

Chart I. Cyclopentadienylmetal Complexes Studied by Chiral HPLC

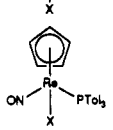
A. Enantiomers Separated on Bakerbond Chiralcel OD

I

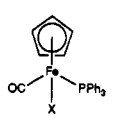
complex	X	lit. ref
1	Me	*a, b*
2	H	*a*
3	F	*c*
4	Cl	*d*
5	Br	*d*
6	I	*d*
7	CO_2Me	*b*
8	OCOMe	*e*
9	$OCOCF_3$	*d*
10	OCOPh	*e*
11	CH_2Ph	*f, b*
12	COPh	*g*
13	Ph	*h*
14	C≡CH	*i, j*
15	C≡CPh	*j, k*
16	C≡CMes	*l*
17	C≡N	*m*
18	Br	*n*
19	COPh	l



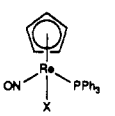
20	Me	*o*
21	C≡N	*o*



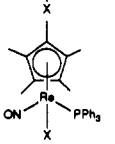
22	I	*p*



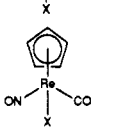
B. Enantiomers Not Separated on Bakerbond Chiralcel OD



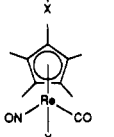
complex	X	lit. ref
23	COMe	*g*
24	COEt	*g*
25	C≡CMe	*j*
26	C≡C^{t}Bu	*i*



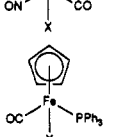
27	Me	*r*
28	CO_2Me	*q*



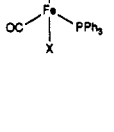
29	Cl	*n*
30	Br	*n*



31	Cl	*n*



32	Me	*s*



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broader than others. Thus, fractions corresponding to the leading (or trailing) edges are likely enriched in one enantiomer.

Discussion

The data in Table I show that the Bakerbond Chiralcel OD HPLC column is broadly applicable for analytical separations of enantiomers of a variety of chiral neutral organorhenium complexes of the formula $(\eta^5\text{-}C_5R_5)Re(NO)(PAr_3)(X)$. The column derives its chirality from a microcrystalline cellulose urethane, which is coated onto silica.

As has been discussed previously, chromatographic methods offer many advantages for the determination of optical purities.[6] Although commercial columns can be expensive (ca. $1000), subsequent costs are low. In particular, we find the accuracy, precision, and speed of analysis to be superior to that attainable polarimetrically or with chiral NMR shift reagents. Furthermore, the amount of sample needed is extremely low.

Several trends emerge from the data in Table I and Chart I. First, enantiomers of alkyl, aryl, and hydride complexes $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(R)$ (**1**, **2**, **11**, and **13**) separate in all cases. Second, enantiomers of halide and pseudohalide adducts $(\eta^5\text{-}C_5H_5)Re(NO)(PPh_3)(X)$ also separate (**3–6**, **8–10**, **17**). Resolution increases in the series I < Br < Cl ≈ F. Although enantiomers of methoxycarbonyl complex **7** and benzoyl complex **12** separate, those of analogous acetyl and propionyl complexes (**23**, **24**) do not. Similarly, enantiomers of alkynyl complexes **14–16** separate, but those of analogous propynyl and 3,3-dimethylbutynyl complexes (**25**, **26**) do not.

Although the resolution is not exceptional, cyanide complex **17** gives the longest retention time of the compounds examined. Interestingly, the enantiomers of **17** are highly differentiated by the chiral NMR shift reagent $Eu(hfc)_3$.[7] With samples of optically active **17**, these two analytical methods give enantiomer ratios that are in excellent agreement.

Pentamethylcyclopentadienyl complexes $(\eta^5\text{-}C_5Me_5)Re(NO)(PPh_3)(X)$ elute much more rapidly than cyclopentadienyl analogues. Although the enantiomers of bromide complex **18** and benzoyl complex **19** separate, enantiomers of other types of complexes resolved in the cyclopentadienyl series do not (**27**, **28**). Note that the resolution observed with **18** and **19** (Table I) is much smaller than that found for cyclopentadienyl analogues **5** and **12**. The tri-*p*-tolylphosphine complexes $(\eta^5\text{-}C_5H_5)Re(NO)(P(p\text{-}tol)_3)(X)$ (**20**, **21**) also elute more rapidly than the PPh_3 analogues. However, enantiomers separate in all cases examined, and the resolution found with cyanide complex **21** is considerably greater than that of PPh_3 analogue **17**.

We are unable to resolve the enantiomers of any carbonyl-substituted complexes $(\eta^5\text{-}C_5R_5)Re(NO)(CO)(X)$ (**29–31**, Chart I part B). We provisionally ascribe this to a requirement for a two-electron donor ligand that is sterically differentiated from NO. However, other explanations are possible. Finally, enantiomers of iron iodide complex $(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)(I)$ (**22**, Chart I part A) separate. However, the resolution is lower than for rhenium analogue **6**, and enantiomers of the corresponding iron methyl complex **32** (Chart I part B) do not separate. Complexes **22** and **32** are, except for a 6–9% contraction in metal–ligand bond lengths, "isosteric" with rhenium analogues **6** and **1**.

We anticipate that significant extensions of the preceding methodology (e.g., related cationic complexes; arene complexes) will be realized in the future, and will report these in our regular research publications.

Experimental Section

Chromatography was conducted on a 10 μM, 4.6 × 250 mm BakerBond Chiracel OD column. Complexes were prepared according to the procedures cited in Chart I. Solvents (EM omnisolve) were filtered through a PALL ultipor N_{66}× 0.45 μm membrane and degassed (sonication, 1 h). The HPLC system consisted of a Waters 590 programmable mobile phase delivery system, a Waters U6K injector, and a Waters lambda-max 481 LC spectrophotometer (set to 280 nm) linked to a HP 3396 integrator. All runs were isocratic.

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Simple Procedure for Conversion of a Trialkyltin Fluoride into the Corresponding Chloride or Bromide

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Summary: Trialkyltin fluorides are converted into the chlorides or bromides on treatment with an excess of the corresponding sodium halide in tetrahydrofuran.

Trialkyltin fluorides are insoluble polymeric solids that can readily be obtained from the chlorides or bromides by shaking these with aqueous alcoholic NaF or KF solutions.[1,2] They have thus been considered to be completely unreactive and therefore useless for synthetic purposes. However, their ready formation has been utilized as a method for removing organotin byproducts formed in organic[3-7] or organometallic[8] syntheses. We now report

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