

## Short Communication

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# High-performance liquid chromatographic separation of chiral metallocenic ketones and alcohols

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### ABSTRACT

The enantiomers of chiral (arene)tricarbonylchromium ketones and alcohols were separated by high-performance liquid chromatography with a Chiralcel OD column. The absolute configuration of the ketones was assigned on the basis of the sign of optical rotation determined with an on-line detector.

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### INTRODUCTION

High-performance liquid chromatography (HPLC) has long been used for the preparative and analytical separation of organometallic compounds. However, in only a few instances has HPLC been applied to the determination of enantiomeric excesses of organometallic derivatives [1].

Recently, the enantiomers of ( $\eta^6$ -benzene)tricarbonylchromium alcohols, methyl esters and acetates and ( $\eta^5$ -cyclopentadienyl)tricarbonylmanganese and ferrocene compounds were separated by HPLC with a Chiralcel OD column [2]. In contrast, this column did not resolve the related aldehydes.

As chiral (arene)tricarbonylchromium ketones are useful starting materials for asymmetric synthesis [3], we have verified if the Chiralcel OD column is suitable for determining their optical purity and

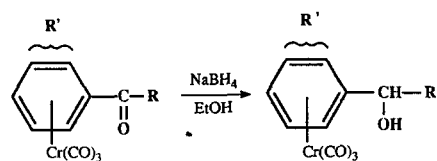
that of the corresponding alcohols obtained by sodium tetrahydroborate reduction.

### EXPERIMENTAL

HPLC was conducted on a 10- $\mu$ m BakerBond Chiralcel OD column (250  $\times$  4.6 mm I.D.), using a Jasco Model 880-PU pump, a Rheodyne Model 7125 injector with a 20- $\mu$ l sample loop, a Jasco 870-UV detector set at 315 nm and a Hewlett-Packard HP-3394A integrator. The order of elution of (arene)tricarbonylchromium ketones was determined employing a Jasco DIP-370 on-line optical rotation detector equipped with a flow cell (5 cm path length) and a solid-state laser beam (670 nm). The system was operated at room temperature at a flow-rate of 0.5 ml/min with 1.5–10% (v/v) ethanol in hexane as the mobile phase.

The Cr(CO)<sub>3</sub> complexes 1–6 were prepared by

complexation of the parent ketones with  $\text{Cr}(\text{CO})_6$  [4]. They were reduced to the corresponding alcohols 7–12 with sodium tetrahydroborate using ethanol as the solvent under nitrogen in the dark. After reaction for 10 min the solvent was evaporated and the residue was diluted with water and extracted with diethyl ether.



1:7a,7b	R = CH <sub>3</sub>	R' = o-CH <sub>3</sub>
2:8a,8b	R = CH <sub>3</sub>	R' = o-OCH <sub>3</sub>
3:9a,9b	R = CH <sub>3</sub>	R' = m-CH <sub>3</sub>
4:10a,10b	R = CH <sub>3</sub>	R' = m-OCH <sub>3</sub>
5:11a,11b	R = C <sub>7</sub> H <sub>15</sub>	R' = o-OCH <sub>3</sub>
6:12a,12b	R = C <sub>7</sub> H <sub>15</sub>	R' = m-CH <sub>3</sub>

Letters a and b refer to the two diastereoisomers differentiated by <sup>1</sup>H NMR spectroscopy on a Bruker AC 300 instrument.

## RESULTS AND DISCUSSION

The racemic  $\text{Cr}(\text{CO})_3$  complexes 1–6 and the corresponding alcohols 7–12 were analysed using the Chiralcel OD column.

The results obtained with the  $\text{Cr}(\text{CO})_3$  ketones are summarized in Table I. The compounds were

completely resolved ( $R_s$  values ranging from 1.01 to 2.22), with the exception of 1. The order of elution of the enantiomers was determined with an on-line optical rotation detector. For *ortho*-substituted ketones the (–)-enantiomer was eluted first and the opposite was found for the *meta*-substituted compounds.

The absolute configuration of *ortho*- and *meta*-substituted complexes 1–6 was assigned on the basis of the model proposed by Solladié-Cavallo [3] for ( $\eta^6$ -arene)tricarbonylchromium ketones. In this model the  $\sigma$  plane of the ring is divided into octants of different size and the signs of optical rotation of the ketones are correlated with the absolute configuration at C-1. It was found that the 1*R*-enantiomers were eluted before the 1*S*-enantiomers (Table I).

The same regularities in the elution order had been already found by Yamazaki *et al.* [2] for organometallic alcohols, acetates and esters; they attributed the planar chirality as “the predominant factor in controlling the binding mode with the substituents of the adsorbent”.

With the alcohols 7–12, which were obtained as diastereomeric mixtures, HPLC was carried out after separation of the diastereoisomers by flash chromatography on silica gel 60 (230–400 mesh, Merck) with mixtures of dichloromethane and diethyl ether as the mobile phase. Table II shows that, with the exception of one diastereoisomer of 10, the resolution of the enantiomers was good to excellent. Therefore, HPLC with Chiralcel OD is very effective.

TABLE I

RESOLUTION OF CHIRAL (ARENE)CARBONYLCHROMIUM KETONES ON CHIRALCEL OD

Compound	Ethanol in hexane (%)	Elution order	$k'{}^a$	$\alpha^b$	$R_s^c$
1	1.5–10		7.56–2.87	1	–
2	6.5	(–)-(R); (+)-(S)	5.78; 6.22	1.08	1.01
3	6.5	(+)-(R); (–)-(S)	3.13; 3.67	1.17	2.06
4	5	(+)-(R); (–)-(S)	3.90; 4.61	1.18	1.93
5	8	(–)-(R); (+)-(S)	2.35; 2.94	1.25	2.22
6	8	(+)-(R); (–)-(S)	1.67; 2.00	1.20	1.25

<sup>a</sup> Capacity factor for the resolved enantiomers. For 1, where there was no enantiomeric resolution,  $k'$  values refer to peak retention as a function of eluent composition.

<sup>b</sup> Separation factor.

<sup>c</sup> Resolution.

TABLE II  
RESOLUTION OF CHIRAL (ARENE)CARBONYLCHROMIUM ALCOHOLS ON CHIRALCEL OD

Compound	Ethanol in hexane (%)	$k'$	$\alpha$	$R_s$
<b>7a</b>	3.3	5.20; 7.10	1.36	4.20
<b>7b</b>	8.3	8.60; 14.41	1.67	6.51
<b>8a</b>	8.5	3.23; 3.52	1.09	0.82
<b>8b</b>	8.5	5.24; 5.90	1.12	1.75
<b>9a</b>	1.5	12.25; 13.50	1.10	1.18
<b>9b</b>	1.5	16.25; 18.25	1.12	1.52
<b>10a</b>	3.5	7.38	1	—
<b>10b</b>	3.5	7.85; 9.67	1.23	4.50
<b>11a</b>	3	0.91; 2.01	2.21	2.03
<b>11b</b>	3	13.70; 14.18	1.04	0.71
<b>12a</b>	2	2.28; 2.46	1.08	0.91
<b>12b</b>	2	2.86; 3.07	1.07	0.63

tive for the separation of racemic chromium-complexed ketones and alcohols and is also simpler than other methods such as  $^1\text{H}$  NMR spectroscopy in the presence of chiral-shift reagents [3].

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