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Asymmetric Oxidation of Sulfenyl Substituted Tricarbonyl(η^6-arene)chromium(0) Complexes

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Abstract: Oxidation of sulfenyl substituted tricarbonyl(η^6-arene)chromium(0) complexes with $Ti(OPr^i)_4$ / diethyl tartrate / H_2O / cumene hydroperoxide (2:4:2:1.3) gives sulfinyl substituted tricarbonyl(η^6-arene)chromium(0) complexes in 60-73% yield and 81-86% e.e. (29-60% yield and 90-≥95% e.e. after crystallisation); diethyl L-(+)-tartrate was shown to lead to complexes of *R* configuration.

For over two decades there has been considerable interest in the application of tricarbonyl(η^6-arene)chromium(0) complexes to problems encountered in organic synthesis.[2] Recently, a substantial proportion of research in this area has been focussed on the discovery and exploitation of reactions of tricarbonyl(η^6-arene)chromium(0) complexes that proceed with high diastereoselectivity,[3] and the design and implementation of efficient routes to optically active complexes. Tricarbonyl(η^6-arene)chromium(0) complexes possessing planar chirality have been generated in enantiomerically enriched form by a) chemical resolution procedures,[4] b) microbial / enzymatic kinetic resolution and desymmetrisation approaches,[5] c) diastereoselective *ortho* lithiations of optically pure tricarbonylchromium(0) complexes of α-methylbenzyldimethylamine,[6] and cyclic acetal, cyclic ketal, and SAMP derivatives of benzaldehyde,[7,8] d) diastereoselective complexation of prochiral arenes carrying an optically pure chiral side-chain,[9] and e) an asymmetric palladium catalysed cross-coupling desymmetrisation of a *meso* complex.[10]

Very recently we reported the first examples of sulfinyl substituted tricarbonyl(η^6-arene)chromium(0) complexes.[11,12] These were synthesised by surprisingly selective and efficient dimethyldioxirane oxidations of the sulfur atoms of sulfenyl substituted complexes. We now wish to report the first examples of optically pure sulfinyl substituted tricarbonyl(η^6-arene)chromium(0) complexes. Although the complexes described herein only currently possess side-chain chirality, we anticipate that interesting applications of these complexes in enantioselective synthesis will soon emerge.

Initial studies involved readily available tricarbonyl[η^6-(methylsulfenyl)benzene]chromium(0) (**1a**) and an [(8,8-dichlorocamphoryl)sulfonyl]oxaziridine reported to give enantioselectivities of 42-74% for the oxidation of sulfides to sulfoxides.[13] As our studies led only to recovered starting material, our attention then turned to other asymmetric oxidising systems and, in particular, Kagan's modified Sharpless reagent.[14] After some experimentation with this system we were pleased to find conditions which enabled us to use this reagent to generate optically enriched sulfinyl substituted complexes.

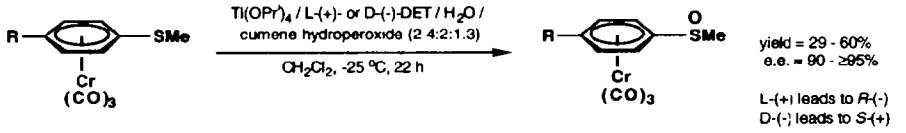
Table Asymmetric oxidation of sulfenyl substituted tricarbonyl(η^6-arene)chromium(0) complexes **1** to sulfinyl substituted complexes **2**[a,b]

entry	sulfenyl complex	diethyl tartrate	sulfinyl complex	before crystallisation		after crystallisation			
				yield(%)	e.e.(%)[c]	yield(%)	e.e.(%)[c]	$[\alpha]_D^{25}$[d]	*R/S*
1	(**1a**)	L-(+)	(-)-(**2a**)	65	83	53	≥95	-208	*R*
2	(**1a**)	D-(-)	(+)-(**2a**)	66	84	37	≥95	+202	*S*
3	(**1b**)	L-(+)	(-)-(**2b**)	73	86	60	90	-170	*R*
4	(**1b**)	D-(-)	(+)-(**2b**)	66	85	29	≥95	+179	*S*
5	(**1c**)	L-(+)	(-)-(**2c**)	60	81	46	≥95	-146	*R*
6	(**1c**)	D-(-)	(+)-(**2c**)	69	82	35	≥95	+147	*S*

[a] Typical asymmetric oxidation procedure (all manipulations were performed under nitrogen using standard vacuum line and Schlenk tube techniques): A solution of diethyl L-(+)-tartrate (0.825 g, 0.68 cm^3, 4.0 mmol) in distilled CH_2Cl_2 (8 cm^3) was cooled to 0 °C and $Ti(OPr^i)_4$ (0.569 g, 0.60 cm^3, 2.0 mmol) was added. The solution was stirred vigorously for 20 min at 0 °C after which H_2O (0.036 g, 36 mm^3, 2 mmol) was added dropwise. After stirring for 30 min at 0 °C, the catalyst was ready to use. A solution of complex (**1a**) (0.260 g, 1.0 mmol) in distilled CH_2Cl_2 (35 cm^3) was stirred at room temperature whilst the catalyst solution was added to it. The catalyst/substrate mixture was then cooled to -25 °C and a mixture of distilled CH_2Cl_2 (5 cm^3) and cumene hydroperoxide (80%, 0.247 g, 0.240 cm^3, 1.3 mmol) was then added dropwise to the cooled reaction mixture over 5 min. The reaction mixture was covered with aluminium foil and maintained at -25 °C for 22 h. Sodium metabisulfite solution (20% w/v, 85 cm^3) was subsequently added to the product mixture at <-20 °C and the mixture was stirred vigorously for 30 min. The aqueous layer was then removed and the resulting yellow gel was transferred onto a pad of Kieselguhr in a fritted funnel. The aqueous layer was extracted with CH_2Cl_2 (20 cm^3) and the extract was added to the filtration column, which was then eluted with CH_2Cl_2. After drying ($MgSO_4$) and removal of the solvent *in vacuo*, the resulting yellow residue was purified by column chromatography (SiO_2; column loaded using Et_2O : CH_2Cl_2, 1:1 and eluted with Et_2O followed by Et_2O : acetone, 9:1) to give a yellow solid (0.178 g, 65%, 83% e.e.). Crystallisation from CH_2Cl_2/petroleum ether (60-80 °C) gave complex (-)-(**2a**) as yellow crystals (0.145 g, 53%, ≥95% e.e.). [b] All new complexes gave satisfactory spectroscopic and microanalytical data. [c] Measured by analysis of the ^1H NMR spectrum obtained by adding 1-2 equivalents of (-)-(*S*)-t-butylphosphinothioic acid to a C_6D_6 solution of the complex. [d] All measurements were taken at 25 °C in acetone (c = 0.01).

Complex (**1a**) was treated with the titanium reagent (formed from 2 equiv. $Ti(OPr^i)_4$, 4 equiv. diethyl L-(+)-tartrate and 2 equiv. of H_2O) and cumene hydroperoxide (1.3 equiv.) at -25 °C for 22 h under nitrogen. After a work-up procedure which included washing with aqueous sodium metabisulfite, the product mixture was chromatographed to remove the diethyl L-(+)-tartrate, unreacted starting material and sulfonyl substituted complex.[15] Every precaution possible was taken to ensure that all the sulfinyl substituted complex (**2a**) was collected from the column. The resulting yellow solid [which represented a 65% yield of (**2a**) and contained only (**2a**) and small amounts (<5%) of decomplexed material] was analysed by ^1H NMR spectroscopy using the chiral solvating reagent (-)-(*S*)-t-butylphenylphosphinothioic acid;[16] the solid was found to have an e.e. of 83%. (1-2 Equivalents of the chiral solvating reagent gave differences in chemical shift of 0.1 - 0.2 ppm for one of the ring protons and up to 0.1 ppm for the methyl group of each of the complexes examined in this study.) Crystallisation of the yellow solid gave a 53% yield of pure crystals of (**2a**) which were essentially optically pure {e.e. ≥ 95% by ^1H NMR spectroscopy; $[\alpha]_D^{25}$ = -208 (c 0.01, acetone)} (Table, Entry 1).

Oxidation of complex (**1a**) in the presence of diethyl D-(-)-tartrate, and the 4-methyl and 4-methoxy substituted complexes (**1b**) and (**1c**) in the presence of either L-(+)- or D-(-)-tartrate gave pleasingly consistent yields and e.e. values before crystallisation (Table, Entries 2-6). Crystallisation led to reduced yields but increased e.e. values.



(**1a-c**) **a**. R = H; **b**: R = Me; **c**: R = MeO (-)- or (+)-(**2a-c**)

In order to determine the absolute stereochemistry of the sulfinyl substituted tricarbonyl(η^6-arene)-chromium(0) complexes (**2a-c**), the sulfinyl substituted complex (-)-(**2a**) was decomplexed with 3 equiv. of ceric ammonium nitrate in methanol at 0 °C for 1 h. Work-up gave a 53% yield of methyl phenyl sulfoxide which was found to have a positive optical rotation {$[\alpha]_D^{25}$ (0.0038, acetone) = +138} {Lit. value:[17] $[\alpha]_D^{24}$ (c ~0.01, absolute EtOH) of (*R*)-phenyl methyl sulfoxide = +149}. Thus it was concluded that the absolute configuration of complex (-)-(**2a**) was *R*, and that the use of diethyl L-(+)-tartrate gives products of *R* configuration whilst the use of diethyl D-(-)-tartrate gives products of *S* configuration. This observation is consistent with the scheme of asymmetric induction proposed by Kagan for the oxidation of uncomplexed alkyl aryl sulfides.[18]

Finally, it is noteworthy that a $Ti(OPr^i)_4$ / diethyl D-(-)-tartrate / H_2O / cumene hydroperoxide oxidation of a sulfenyl substituted ferrocene has recently been reported; this gave a 55% yield and 90% e.e. of a sulfinyl substituted ferrocene product of *S* configuration.[19]

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