A Dimethyldioxirane-mediated Route to Enantiomerically Pure Tricarbonylchromium(0) Complexes of *ortho*-Substituted Styrenes

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Dimethyldioxirane oxidation of tricarbonylchromium(0) complexes of a range of *ortho*-substituted (*S*)-α-methylbenzyldimethylamines **3a–f** proceeds smoothly to give enantiomerically pure tricarbonylchromium(0) complexes of *ortho*-substituted styrenes **4a–f** *via* chemoselective oxidation of the tertiary amines to their *N*-oxides and subsequent Cope reactions.

For over two decades there has been considerable interest in the application of tricarbonyl(η⁶-arene)chromium(0) complexes to problems encountered in organic synthesis.[1] A significant proportion of the recent research in this area has been focused on the design and implementation of efficient routes to optically active complexes. Currently, the main approaches to enantiomerically enriched tricarbonyl(η⁶-arene)chromium(0) complexes possessing planar chirality are (*a*) chemical resolution,[2] (*b*) microbial/enzymatic kinetic resolution and desymmetrisation,[3] and (*c*) diastereoselective ortholithiation of optically pure tricarbonylchromium(0) complexes of either α-methylbenzyldimethylamine **1**,[4] or cyclic acetal and ketal derivatives of benzaldehyde and acetophenone.[5,6] Approach (*c*) readily gives products of very high enantiomeric purity and, in the latter cases, a synthetically useful carbonyl functional group is accessible from the products.

We are currently interested in the use of dimethyldioxirane in organometallic chemistry and we have recently demonstrated that this reagent selectively oxidises sulfides to sulfoxides in the presence of the oxidation-sensitive tricarbonylchromium(0) moiety.[7] We now present results which not only demonstrate that dimethyldioxirane may be used to oxidise amines and phosphines to their respective oxides in the presence of a low-valent transition metal, but also represent an efficient route to optically pure tricarbonyl(η⁶-arene)chromium(0) complexes bearing potentially versatile vinyl groups.†

(*S*)-α-Methylbenzyldimethylamine **1**, derived from (*S*)-α-methylbenzylamine, was readily converted into its tricarbonylchromium(0) complex **2** in 87% yield by heating with $Cr(CO)_6$ (2.5 equiv.).[4] In our initial studies, complex **2** was then converted into complex **3a** (E = SMe) in 81% yield by treatment with Bu^{t}Li followed by MeS–SMe (Table 1, entry 1). The introduction of the methylsulfenyl *ortho* substituent proceeded diastereospecifically (≥96% d.e., the minor diastereoisomer could not be observed by 270 MHz ^{1}H NMR spectroscopy of the crude product) and the stereochemistry of **3a** was assigned using a model proposed previously to explain the selectivity of analogous deprotonation/electrophilic quench manipulations of complex **2**.[4]

Oxidation of complex **3a** with dimethyldioxirane was then examined. Whilst oxidation of **3a** with 1.2 equiv. of dimethyldioxirane resulted in a chemoselective and highly diastereoselective oxidation of the sulfenyl substituent to the corresponding sulfinyl substituent as anticipated[7] (66% yield, d.e. ≥96%), oxidation of **3a** with 2.4 equiv. of dimethyldioxirane gave a quite different product which was identified from its spectroscopic data‡ as complex **4a** (80% yield). These observations reveal that the second equivalent of dimethyldioxirane oxidises the tertiary amine present in complex **3a** to its amine oxide which subsequently undergoes a Cope reaction under remarkably mild conditions to give the vinyl substituent observed in the product.§

Similar results were obtained with a range of *ortho* substituents. Introduction of phosphorus, silicon, iodine and carbon substituents into complex **2** proceeded smoothly and diastereoselectively (≥96% d.e. in all cases) to give complexes **3b–e** (see Table 1), and oxidation of all of these complexes with dimethyldioxirane gave the corresponding *ortho*-substituted styrene complexes in 48–80% yield (see Table 1). (It is of note that formation of the styrene complex from phosphine **3b** required 2.4 equiv. of dimethyldioxirane as 1.2 equiv. selectively oxidised the phosphorus to give the corresponding phosphine oxide complex in 77% yield.) Similarly complex **3f** [E = (*Z*)–CH=CH–CH=CH_2] (formed from complex **2** *via* a

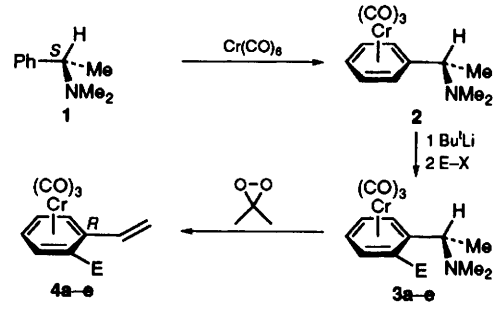

Table 1 Elaboration of complex **2** to the *ortho*-substituted complexes **3a–e** and their dimethyldioxirane-mediated oxidation[a] to the styrene complexes **4a–e**

Entry	Electrophile (E–X)	Complex **3**	Yield (%)	Complex **4**	Yield (%)
1	MeS–SMe	**3a**	81	**4a**[b]	80
2	Ph_2P–Cl	**3b**	69	**4b**[c]	73
3	Me_3Si–Cl	**3c**	70	**4c**	69
4	I–CH_2CH_2I	**3d**	83	**4d**	48
5	H_2C=$CHCH_2$–Br	**3e**[d]	70	**4e**	65

[a] Typical oxidation procedure: dimethyldioxirane [8.2 cm^3 of a 0.082 mol dm^{-3} solution diluted with nitrogen-saturated acetone (5 cm^3), 0.67 mmol], precooled to −78 °C, was added dropwise *via* a cannula to a yellow solution of complex (+)-**3c** (0.20 g, 0.56 mmol) in nitrogen-saturated acetone (10 cm^3) in a Schlenk tube at −78 °C. The reaction mixture was stirred for 15 min at −78 °C and then removed from the cooling bath and stirred for a further 2 h. The solvent was removed *in vacuo* from the resulting yellow-pale green product mixture and the resulting residue was filtered through Kieselguhr using diethyl ether as eluent. Column chromatography [SiO_2; diethyl ether–light petroleum (bp 60–80 °C), 1:9] gave an orange–yellow solid which was crystallised from hexane to give the enantiomerically and analytically pure styrene complex **4c** as orange–yellow needles (0.12 g, 69%). [b] E = S(O)Me; 2.4 equiv. of dimethyldioxirane used in oxidation. [c] E = P(O)Ph_2; 2.4 equiv. of dimethyldioxirane used in oxidation. [d] 1.1 equiv. CuBr·SMe_2 added after Bu^{t}Li in preparation of **3e**.

diastereoselective *ortho* formylation and a Wittig reaction) was oxidised to triene **4f** [E = (*Z*)-CH=CH-CH=CH_2] in 64% yield.

Consideration of the stereochemical aspects of the reactions involved in the conversion of (*S*)-α-methylbenzylamine into the *ortho*-substituted styrene complexes **4a–f** suggests that complexes **4a–f** should be enantiomerically pure. Chiral HPLC analysis¶ of samples of complex **4c** derived from both (*S*)- and racemic α-methylbenzylamine confirmed that the material derived from (*S*)-α-methylbenzylamine was indeed optically pure {e.e. ≥99%; $[\alpha]_D^{27.5} = -568.7$ (*c* 1, $CHCl_3$)}. thus the cheap 'chiral pool' tetrahedral chirality of (*S*)-α-methylbenzylamine has been cleanly transformed into planar chirality in the *ortho*-substituted styrene complexes **4a–f**. The reactivity of the alkene in complexes **4a–f** is currently under investigation.

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Footnotes

† Palladium catalysed cross-coupling of tricarbonyl(*o*-dichlorobenzene)chromium(0) with vinyl metal reagents in the presence of chiral ligands has recently been shown to generate tricarbonyl(*o*-chlorostyrene)chromium(0) in up to 44% e.e.[8]

‡ All novel complexes (**3a**, **3d–f** and **4a–f**) gave satifactory spectroscopic (IR, ^{1}H NMR, ^{13}C NMR and low-resolution MS) and microanalytical or high-resolution MS data.

§ It is interesting to compare the mild conditions used in this formal elimination of dimethylamine with the relatively harsh conditions used in a recently reported formal elimination of dimethylamine from an *ortho*-substituted dimethyl(1-ferrocenylethyl)amine [*i.e.* trichloromethyl chloroformate (diphosgene) in refluxing toluene].[9]

¶ CHIRALCEL OD-H, Daicel Chemical Industries; hexane–isopropanol (99 : 1), 0.5 ml min^{-1}.

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