

Sulfoxides and stereochemical control in organometallic chemistry

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Abstract - The sulfinyl substituted oxadienes [RS(O)CH=CHC(Me)=O; R = Bu^t, Ph] form stable diastereoisomerically pure tricarbonyliron(0) complexes, the relative stereochemistry of which was determined by X-ray crystal structure analysis. Phenylsulfinylethene forms a stable tetracarbonyliron(0) complex which is also diastereoisomerically pure. An X-ray crystal structure analysis of this complex revealed its relative stereochemistry and evidence for a through-space interaction between the oxygen atom of the sulfinyl substituent and the carbon atom of one of the metal carbonyl ligands. Dimethyldioxirane efficiently oxidises tricarbonylchromium(0) complexes of sulfenyl substituted arenes to tricarbonylchromium(0) complexes of sulfinyl substituted arenes. The diastereoselectivity of the oxidation of *ortho* substituted complexes was determined and found to be dramatically reversed when the sulfenyl substituent is changed from methyl to *tert*-butyl.

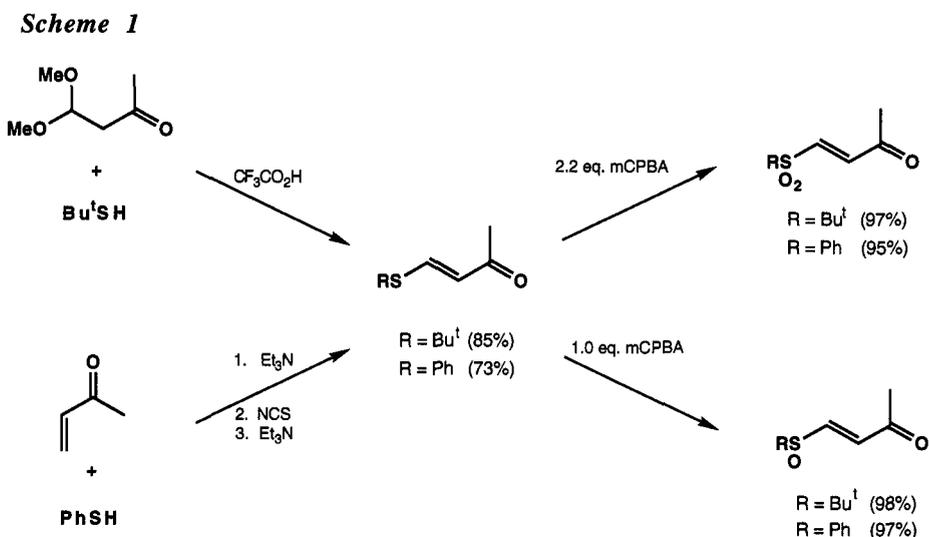
INTRODUCTION

In recent years there has been widespread interest in the use of sulfinyl substituents to control the chemical and stereochemical outcome of organic reactions. In particular, the unique stereochemical properties of the sulfinyl group have attracted many organic chemists and numerous methods for exploiting its chirality have been developed (ref. 1). In contrast the use of sulfinyl substituted ligands in organometallic chemistry is as yet essentially unexplored and unexploited, although a recent asymmetric synthesis and highly diastereoselective *ortho*-lithiation of ferrocenyl sulfoxides (ref. 2) is of note in this context. In this paper, we describe stereochemical aspects of two organometallic systems bearing sulfinyl substituted ligands. In the first, complexation of sulfinyl substituted ligands to iron carbonyl fragments produces diastereoisomerically pure organoiron complexes (ref. 3), whilst in the second, oxidation of a sulfenyl group on a chiral complex leads to sulfinyl substituted organochromium complexes of high diastereoisomeric purity (ref. 4).

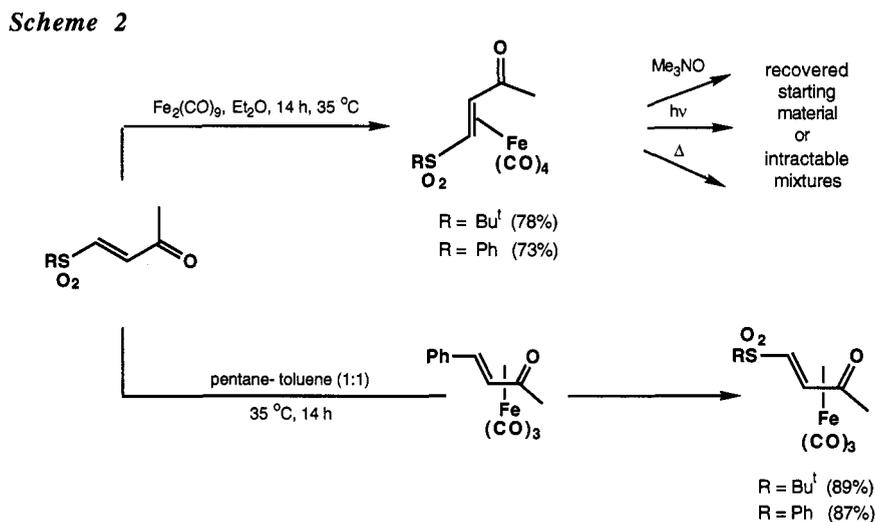
SULFINYL-CONTROLLED FORMATION OF TRICARBONYL(OXADIENE)-IRON(0) COMPLEXES AND A TETRACARBONYL(ALKENE)IRON(0) COMPLEX

As sulfinyl groups often exert good stereocontrol over the formation of new chiral centres in organic systems, we wished to determine whether or not the sulfinyl group could control the formation of new metal-centred elements of chirality in organometallic systems. Due to our ongoing interest in the reactivity of tricarbonyl(oxadiene)iron(0) complexes (ref. 5), the first systems that we examined were β -sulfinyl substituted vinyl ketones. In the course of our studies, we also investigated the reactivity of the corresponding β -sulfenyl and β -sulfonyl compounds, as we anticipated that their reactivity might shed some light on the behaviour of the β -sulfinyl compounds.

The β -sulfenyl vinyl ketones, 4-(*tert*-butylsulfenyl)but-3-en-2-one and 4-(phenylsulfenyl)but-3-en-2-one, were readily synthesised using literature procedures (scheme 1) (ref. 6). Oxidation of the sulfenyl substituents with 2.2 equiv. of 98% *m*CPBA gave sulfonyl substituted vinyl ketones, and oxidation of the sulfenyl substituents with 1.0 equiv. of 98% *m*CPBA gave sulfinyl substituted vinyl ketones.

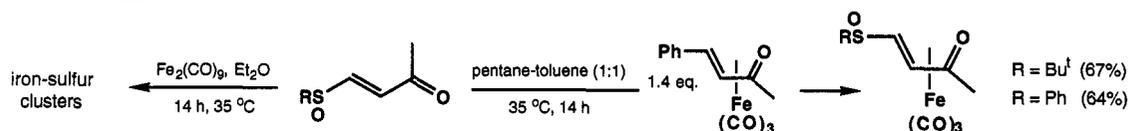


The formation of iron carbonyl complexes from the β -sulfenyl, β -sulfonyl and β -sulfinyl vinyl ketones was then addressed. Attempts to form complexes from the β -sulfenyl vinyl ketones were unsuccessful: although many reaction conditions were examined, the only products generated were iron-sulfur clusters. Attention then turned to the β -sulfonyl vinyl ketones. Reacting these with $\text{Fe}_2(\text{CO})_9$ gave compounds which were identified as tetracarbonyl(alkene)iron(0) complexes rather than the desired tricarbonyl(oxadiene)iron(0) complexes. Attempts to decarbonylate the tetracarbonyl complexes using standard methods led either to the recovery of starting material or intractable mixtures, and so we reasoned that the use of a source of the required tricarbonyliron(0) unit in the complexation step may provide a more successful route to the target tricarbonyliron(0) complexes. Indeed, the β -sulfonyl vinyl ketones reacted with tricarbonyl(benzylideneacetone)iron(0) under remarkably mild conditions to give stable crystalline tricarbonyl(oxadiene)iron(0) complexes in excellent yield (scheme 2).



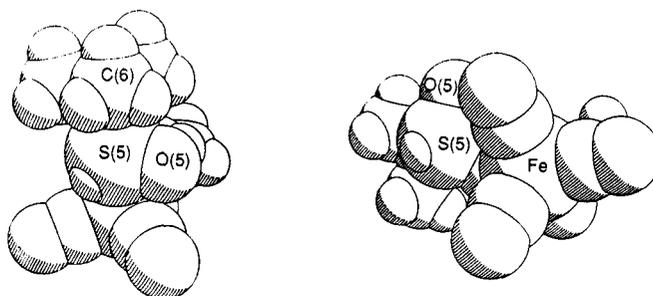
As it had been established that β -sulfenyl substituted vinyl ketones do not form stable tricarbonyliron(0) complexes whilst β -sulfonyl substituted vinyl ketones form very stable complexes in high yield, it was unclear whether or not the intermediate and stereochemically more interesting β -sulfinyl substituted vinyl ketones would form stable tricarbonyliron(0) complexes. Although the β -sulfinyl vinyl ketones only gave iron-sulfur clusters when treated with $\text{Fe}_2(\text{CO})_9$, we were pleased to find that they reacted with tricarbonyl(benzylideneacetone)iron(0) to give stable tricarbonyl(oxadiene)iron(0) complexes in good, but perhaps significantly reduced yield relative to the sulfonyl systems (scheme 3).

Scheme 3



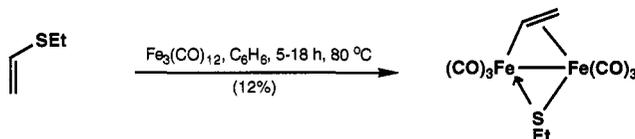
More significantly, careful examination of the ^1H NMR spectroscopic data of the crude products and of the pure products revealed that in each complexation, only one diastereoisomer had been produced. The relative stereochemistry of the single diastereoisomer produced by transfer of the tricarbonyliron(0) unit from the benzylideneacetone complex to 4-(*tert*-butylsulfinyl)but-3-en-2-one was determined by an X-ray crystal structure analysis (scheme 4). This revealed that in the diastereoisomer formed, the oxygen of the sulfinyl group is placed surprisingly close to a metal carbonyl ligand whilst the sterically less demanding sulfinyl lone pair lies between two metal carbonyl ligands. This led us to postulate that there is a weak interaction between the oxygen of the sulfoxide and the carbon of the appropriate carbonyl ligand that gives rise to the observed diastereoselectivity in this system. Measurement of this oxygen-carbon distance [3.12 Å (the sum of the van der Waals radii of oxygen and carbon is approximately 3.1 Å)] and the iron-carbon-oxygen bond angles of the three metal carbonyl ligands [178.2(5), 177.8(5) and 179.3(5)], however, provided no evidence for such an interaction.

Scheme 4



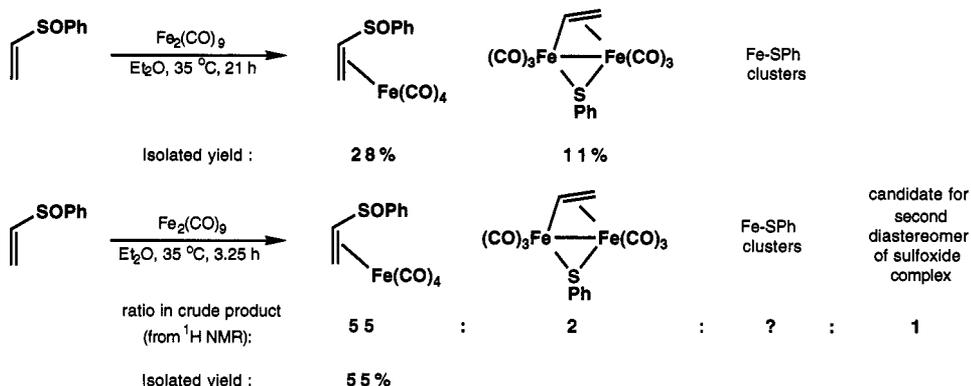
Having discovered that complexation of β -sulfinyl substituted vinyl ketones leads to diastereoisomerically pure organoiron compounds, we were naturally interested to determine whether or not other sulfinyl substituted ligands would behave similarly. Thus we turned our attention to sulfinyl substituted alkenes and the formation of tetracarbonyl(alkene)iron(0) complexes. As before, the reactivity of the sulfinyl systems was compared with the reactivity of the corresponding sulfenyl and sulfonyl systems. The addition of $\text{Fe}_3(\text{CO})_{12}$ to various sulfenyl substituted alkenes had been investigated many years ago and shown to produce *inter alia* dimetallic iron species in which a tricarbonyliron(0) unit has inserted into the sp^2 -carbon sulfur bond of the organic substrate (scheme 5) (ref 7).

Scheme 5



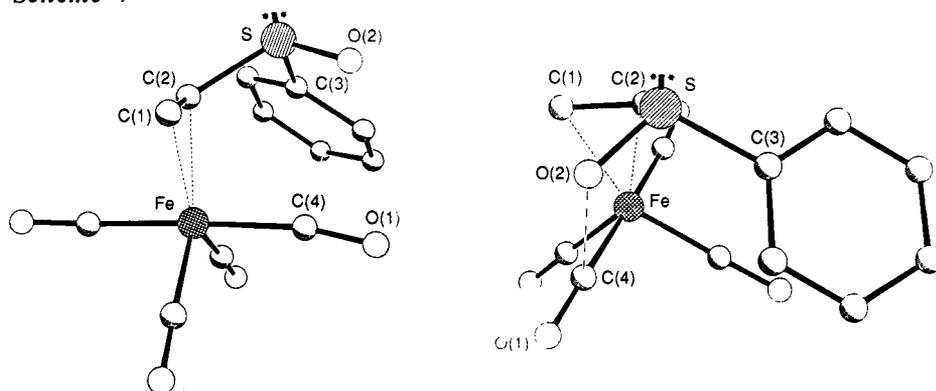
After finding that phenylsulfonylene reacted readily with $\text{Fe}_2(\text{CO})_9$ to give a very stable crystalline tetracarbonyl(alkene)iron(0) complex in 92% yield, we then examined the reaction between $\text{Fe}_2(\text{CO})_9$ and phenylsulfinylethene. In the first experiment performed, phenylsulfinylethene was stirred with $\text{Fe}_2(\text{CO})_9$ at 35 °C for 21 h. Column chromatography of the product mixture led to the isolation of the required tetracarbonyl(alkene)iron(0) complex, a dimetallic species analogous to the ones isolated from the sulfenyl substituted alkene reactions, and iron-sulfur clusters (scheme 6). The reaction was repeated but this time it was only allowed to proceed for 3.25 h. Analysis of the crude product by ^1H NMR spectroscopy showed that it contained the required tetracarbonyl complex and the di-iron species in a 55:2 ratio. The spectrum also contained evidence for the presence of small amounts of iron-sulfur clusters and small signals which could possibly be attributed to the minor diastereoisomer.

Scheme 6



It proved possible to isolate diastereoisomerically pure tetracarbonyl(phenylsulfinylethene)iron(0) in 55% yield and this was examined by X-ray crystallography in order to determine the relative stereochemistry of the sulfinyl substituent and the iron carbonyl unit (scheme 7). In this case, good evidence was found for a through-space interaction between the oxygen atom of the sulfinyl group [O(2)] and the carbon atom of one of the iron carbonyl ligands [C(4)]. The distance between the two atoms was found to be 2.76Å (considerably less than the sum of their van der Waals radii of ~3.1Å). Furthermore, the carbonyl group with which the sulfinyl oxygen appears to be interacting is significantly more bent than the three other metal carbonyl ligands. The Fe-C(4)-O(1) bond angle was found to be 170.4(4) $^\circ$ whilst the three remaining carbonyl ligands were found to have Fe-C-O angles of 178.5(3), 178.4(4) and 177.8(4) $^\circ$. It was also noted that the sulfur lone pair in the complex is directed away from the metal centre in the diastereoisomer formed. This observation led us to postulate that the diastereochemical purity of the complex produced in the complexation reaction may arise from destruction of the other diastereoisomer. This could occur by interaction of the sulfur lone pair of the other diastereoisomer with suitable metal orbitals leading to the insertion of the iron atom into the C(2)-S bond to give the dimetallic complex and ultimately the iron-sulfur clusters observed. The sulfinyl oxygen-carbonyl carbon interaction that occurs in the isolated diastereoisomer may be preventing rotation around the C(2)-S bond and hence the interaction of the sulfur lone pair with the iron centre.

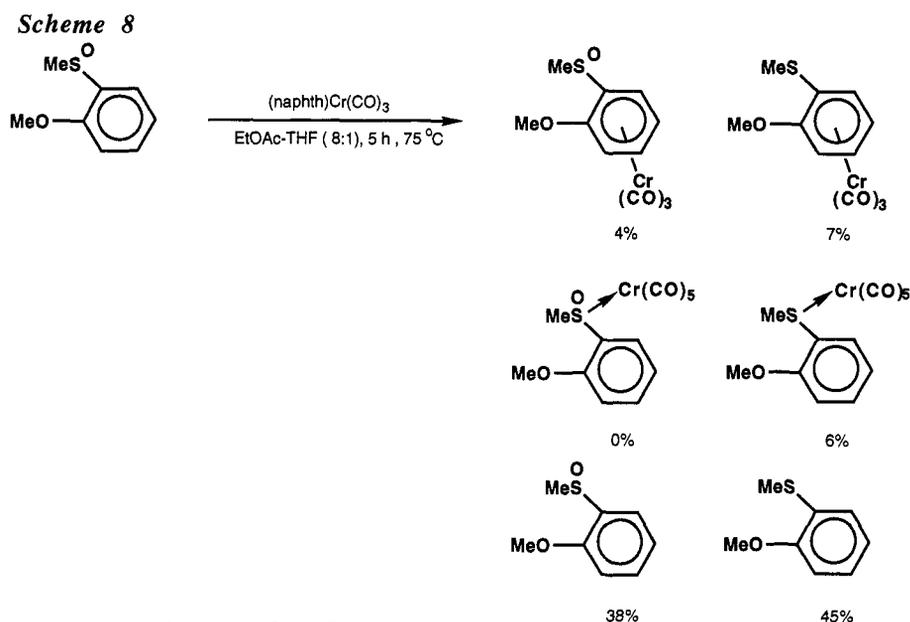
Scheme 7



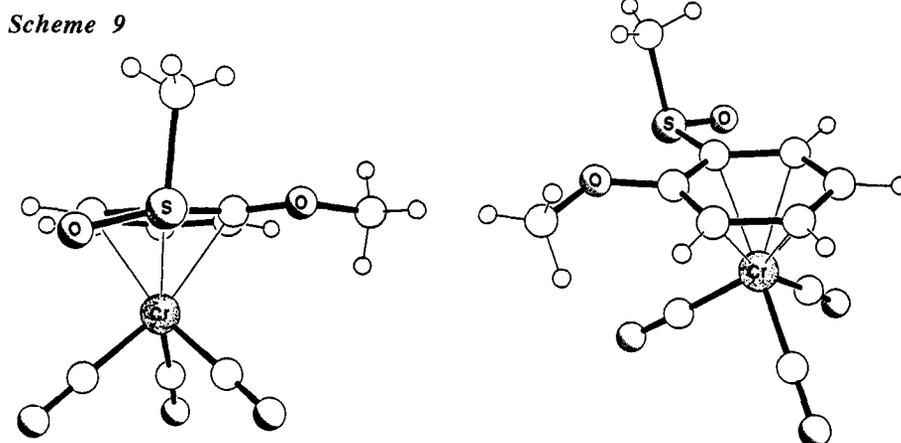
OXIDATION OF SULFENYL SUBSTITUTED TRICARBONYL(ARENENE)-CHROMIUM(0) COMPLEXES TO SULFINYL SUBSTITUTED TRICARBONYL(ARENENE)CHROMIUM(0) COMPLEXES

In order to increase our knowledge of how sulfinyl substituted ligands interact with metal carbonyl groups, we wished to synthesise tricarbonylchromium(0) complexes of sulfinyl substituted arenes. We were considerably surprised, however, to find that despite the long standing interest in the application of tricarbonyl(arene)chromium(0) complexes to problems encountered in organic synthesis (ref. 8) and the current widespread interest in the stereochemical properties of these complexes (refs. 9 and 10), tricarbonylchromium(0) complexes of sulfinyl substituted arenes had not been reported in the literature.

In order to relate any results obtained to those obtained with the iron systems, our initial efforts to form a tricarbonylchromium(0) complex of a sulfinyl substituted arene focussed on direct complexation of sulfinyl substituted arenes. Accordingly, 2-methoxy-1-(methylsulfinyl)benzene and 3-methoxy-1-(methylsulfinyl)benzene were synthesised and reacted with a range of reagents routinely used for the formation of tricarbonyl(arene)chromium(0) complexes. The results were disappointing - reacting the arenes with $\text{Cr}(\text{CO})_6$ or $\text{Cr}(\text{CO})_3(\text{pyridine})_3$ gave none of the required sulfinyl substituted complexes, whilst reacting the *ortho*-substituted arene (but not the *meta*-substituted arene) with tricarbonyl(naphthalene)chromium(0) or $\text{Cr}(\text{CO})_3(\text{MeCN})_3$ gave only trace amounts of the sulfinyl substituted complex. A typical result is illustrated below (scheme 8).



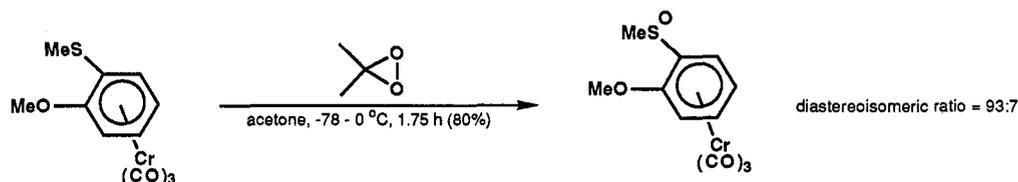
Although the reactions between 2-methoxy-1-(methylsulfinyl)benzene and tricarbonyl(naphthalene)chromium(0) or $\text{Cr}(\text{CO})_3(\text{MeCN})_3$ had produced only trace amounts of sulfinyl substituted complex, only one diastereoisomer of the complex had been formed in each case. In order to determine its relative stereochemistry, the reaction between the arene and $\text{Cr}(\text{CO})_3(\text{MeCN})_3$ was repeated on a larger scale and the complex was isolated, fully characterised and examined by X-ray crystallography (scheme 9).



As the yield of tricarbonyl[2-methoxy-1-(methylsulfinyl)benzene]chromium(0) was both poor and capricious, an alternative route to tricarbonylchromium(0) complexes of sulfinyl substituted arenes was sought. It has been known for some time that sulfonyl substituted arenes readily form tricarbonylchromium(0) complexes (ref. 11), and so oxidation of sulfinyl substituents was proposed as a potentially much more efficient route to tricarbonylchromium(0) complexes of sulfinyl substituted arenes. Thus 2-methoxy-1-(methylsulfonyl)benzene was converted into its tricarbonylchromium(0) complex in 89% yield by heating it

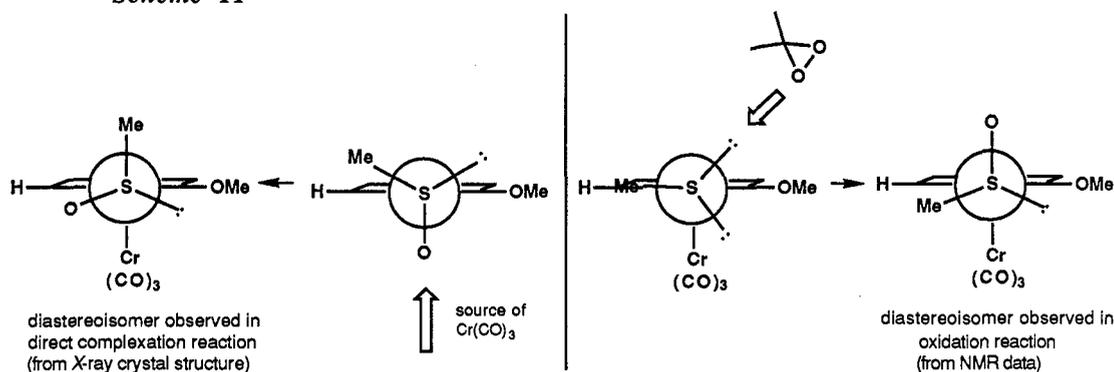
with $\text{Cr}(\text{CO})_6$. Initial experiments were discouraging: oxidation of the sulfenyl substituted complex with *m*CPBA, *tert*-butyl hydroperoxide and 2-hydroperoxy-2-methoxypropane led essentially to decomplexation of the tricarbonylchromium(0) unit and the isolation of metal-free arenes. Attention then turned to dimethyldioxirane, a reagent which has rapidly been accepted as a useful mild oxidant for many organic transformations and which is beginning to prove very useful for organometallic transformations. Pleasingly, oxidation of tricarbonyl[2-methoxy-1-(methylsulfenyl)benzene]chromium(0) with 1.1 equiv. of dimethyldioxirane led to the formation of the required sulfoxide complex in good yield. Moreover the complex was formed with high diastereoselectivity (diastereoisomeric ratio = 93:7) (scheme 10).

Scheme 10



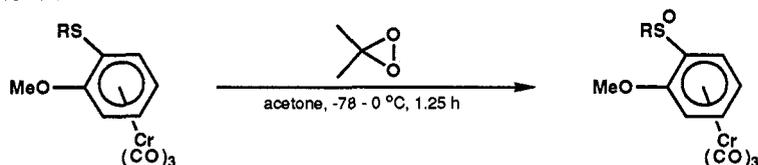
The major diastereoisomer formed by oxidation proved to be the opposite diastereoisomer to the one formed by direct complexation and this was rationalised in the manner illustrated below (scheme 11).

Scheme 11



In order to determine whether or not the diastereoisomeric ratio of 93:7 observed in the oxidation of the methylsulfenyl substituted complex could be improved significantly by increasing the size of the alkyl group of the sulfenyl substituent, the corresponding *tert*-butylsulfenyl substituted complex was synthesised and oxidised. Oxidation using dimethyldioxirane gave a crude product which contained only one sulfoxide complex (scheme 12). Subsequent crystallisation of the crude product gave the pure sulfinyl substituted complex in 77% yield. Interestingly, an *X*-ray crystal structure analysis of this material revealed that its relative stereochemistry was the same as the relative stereochemistry of the methylsulfenyl substituted complex formed by direct complexation *i.e.* oxidation of the methylsulfenyl and the *tert*-butylsulfenyl substituted complexes had proceeded with complementary selectivity.

Scheme 12

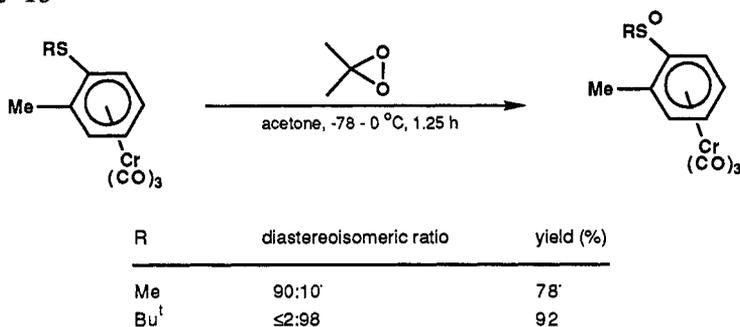


R	diastereoisomeric ratio	yield of major diastereoisomer (%)
Me	93:7	80
Et	85:15	39
Pr [†]	30:70	56
Bu [†]	≤2:98	77

To investigate this interesting reversal of stereoselectivity in more detail, the corresponding ethylsulfenyl and *iso*-propylsulfenyl substituted complexes were synthesised and oxidised. Oxidation of the ethylsulfenyl substituted complex gave predominantly the same diastereoisomer as the methylsulfenyl substituted system (as confirmed by an X-ray crystal structure analysis of this product), whilst oxidation of the *iso*-propylsulfenyl substituted complex gave predominantly the same diastereoisomer as the *tert*-butylsulfenyl substituted system (scheme 12).

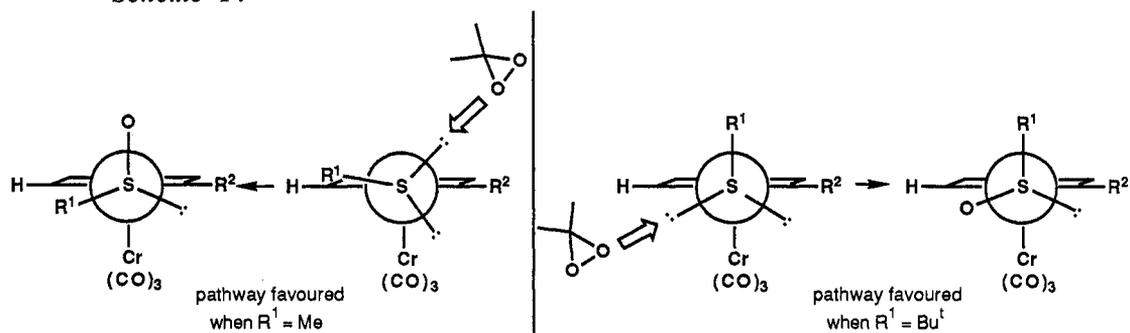
Next the *ortho*-methoxy substituent was replaced by a methyl group in order to gain some insight into whether or not the observed change in diastereoselectivity was electronic or steric in nature. Oxidation of the appropriate methylsulfenyl and *tert*-butylsulfenyl systems proceeded in a similar manner to the methoxy substituted cases giving opposite diastereoisomers with good stereoselectivity (scheme 13). This is consistent with steric factors governing the stereoselectivity of the system.

Scheme 13



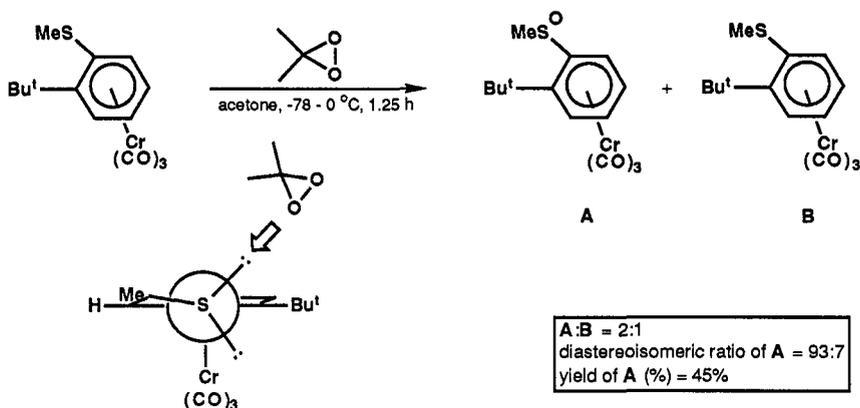
An explanation for the dramatic difference in diastereoselectivity between the methylsulfenyl substituted complexes and the *tert*-butylsulfenyl substituted complexes is illustrated below (scheme 14). When $R^1 = \text{Me}$, eclipsing interactions between the methyl group and the hydrogen *ortho* to the sulfenyl group are inconsequential and so the methylsulfenyl substituted complex can adopt a conformation in which one of the sulfur lone pairs is exposed on the *exo* face of the complex. Oxidation of this lone pair leads to the observed diastereoisomer. When $R^1 = \text{Bu}^t$, however, eclipsing interactions between the *tert*-butyl group and the *ortho* hydrogen, the R^2 substituent and the tricarbonylchromium(0) fragment, restrict the *tert*-butylsulfenyl substituent to the conformation illustrated, in which neither of the sulfur lone pairs is on the *exo* face of the complex. Consequently the dioxirane is forced to approach the *endo* face of the complex past the least sterically demanding *ortho* substituent to give the other diastereoisomer. The cases where $R^1 = \text{Et}$ and Pr^i represent intermediate situations in which the energy differences between the transition states leading to the two diastereoisomers are less pronounced.

Scheme 14



Finally, the effect of increasing the size of the *ortho* substituent, R^2 , was examined. Oxidation of tricarbonyl[2-*tert*-butyl-1-(methylsulfenyl)benzene]chromium(0) under identical conditions used for all the other oxidations gave a crude product containing not only the sulfinyl substituted complex dominated by the diastereoisomer consistently formed on oxidation of methylsulfenyl substituted complexes, but also significant quantities of starting material (scheme 15). Thus when $R^2 = \text{Bu}^t$ rather than MeO or Me, the rate of oxidation is significantly retarded and this is attributed to the increased energy required for the dimethyldioxirane to approach the *exo* lone pair of the conformation illustrated past the relatively sterically demanding *tert*-butyl group.

Scheme 15



CONCLUSIONS

The results presented in this paper reveal that providing appropriately mild reaction conditions and/or suitably selective reagents are used in their synthesis, sulfinyl groups and low-valent metal carbonyl fragments are compatible. Moreover, our results suggest that the stereochemical properties of organometallic complexes of sulfinyl substituted ligands should prove to be just as fascinating as their organic counterparts.

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