Asymmetric Synthesis of Phenyl Alkyl Sulphoxides *via* the Non-destructive Mediation of the Chiral Iron Acyl [(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2Me$]

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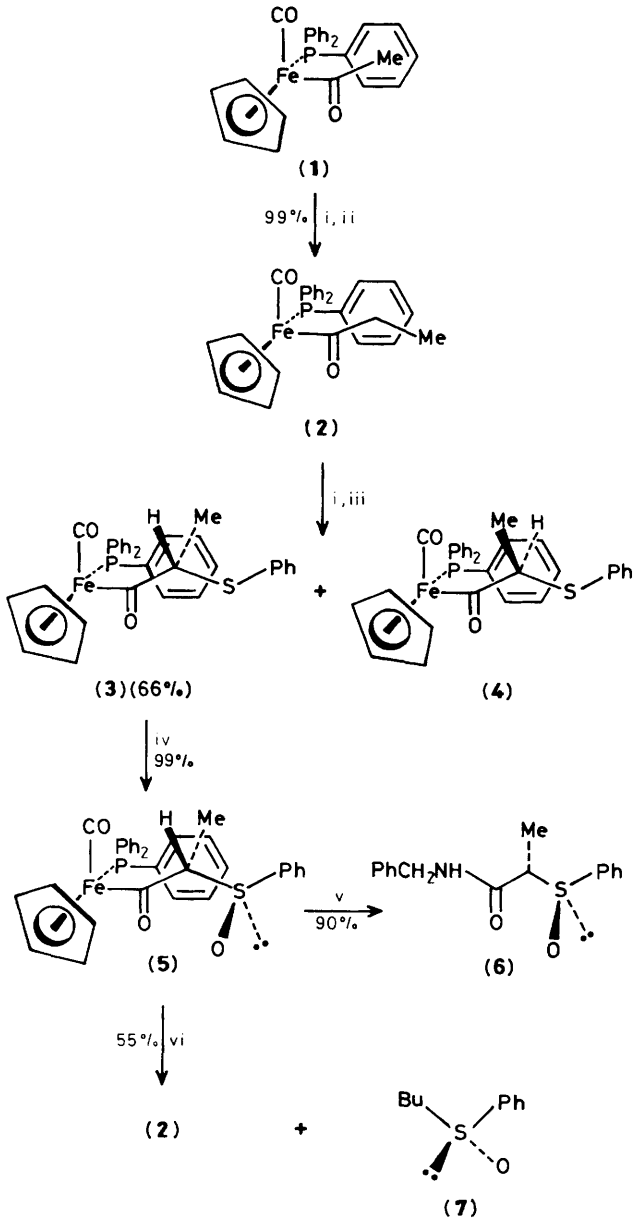
The chiral sulphoxide (*RSS*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCHMeSOPh] can be efficiently and stereoselectively prepared from (*R*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2Me$] *via* the asymmetric oxidation of the corresponding sulphide: treatment of (*RSS*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCHMeSOPh] with lithium dialkylcuprates afforded phenyl alkyl sulphoxides and regenerated (*R*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2Me$], while oxidative decomplexation led to (*SS*)-$PhCH_2NHCOCHMe$-SOPh; all the products were essentially enantiomerically pure.

Chiral sulphoxides, as well as being pharmacologically interesting in their own right,[1] are proving to be increasingly useful as chiral auxiliaries.[2] Almost without exception, the synthesis of optically active sulphoxides has been *via* the resolution of menthylsulphinate esters.[3] To date, no general method for the direct synthesis of enantiomerically pure sulphoxides has been reported, although Kagan[4] and others[5] have developed protocols for the highly stereoselective [<96% enantiomeric excess (e.e.)] oxidation of certain aryl alkyl sulphides to the corresponding sulphoxides. In this



Scheme 1. *Reagents:* i, BuLi; ii, MeI; iii, PhSSPh; iv, *m*CPBA, tetrahydrofuran; v, NBS, $PhCH_2NH_2$; vi, $LiCuBu_2$.

communication we report the asymmetric synthesis of chiral phenyl alkyl sulphoxides *via* the non-destructive mediation of the iron acyl $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2Me]$.[6]

Methylation of the enolate derived from (*R*,*S*)-acetyl complex (**1**)† proceeded essentially quantitatively to generate the (*R*,*S*)-propionyl complex (**2**) (Scheme 1). Trapping of the (*E*)-enolate derived from (**2**)[6] with diphenyl disulphide occurred stereoselectively producing a 16:1 mixture of the (*RS*,*SR*)-(**3**)‡ and (*RR*,*SS*)-(**4**) diastereoisomers. The relative stereochemistries of (**3**) and (**4**) were assigned on the basis of the ^{1}H n.m.r. chemical shifts of the methyl groups at δ 0.62 and 1.43, respectively.[6] A single crystallisation gave (*RS*,*SR*)-(**3**) diastereoisomerically pure in 66% yield. Oxidation of (**3**) with *m*-chloroperbenzoic acid (*m*CPBA) at −100 °C gave stereoselectively the corresponding sulphoxide (**5**) as a single diastereoisomer in essentially quantitative yield. The relative stereochemistry of (**5**) was assigned as (*RSS*,*SRR*) by *X*-ray crystal structure analysis.[7] Repetition of the above synthetic sequence starting from the optically pure acetyl complex (*R*)-(**1**)[6] yielded enantiomerically and diastereoisomerically pure (*RSS*)-(**5**), *via* (*R*)-(**2**) {$[\alpha]_D$ −185° (*c* 0.041, C_6H_6)}.

Oxidative decomplexation of (**5**) with *N*-bromosuccinimide (NBS) in the presence of benzylamine gave the (*SS*)-β-sulphinylamide (**6**) {$[\alpha]_D$ −184° (*c* 4.77, EtOH)}. ^{1}H N.m.r. analysis of (−)-(**6**) compared with (±)-(**6**) in the presence of the chiral shift reagent (−)-2,2,2-trifluoro-1-(9-anthryl)-ethanol was consistent with (−)-(**6**) being enantiomerically pure.

Treatment of (*RSS*)-(**5**) with lithium dibutylcuprate gave a mixture, which was readily separable by chromatography, of starting material (*RSS*)-(**5**), the propionyl complex (*R*)-(**2**), and (*R*)-phenyl butyl sulphoxide (**7**). The corrected yield of sulphoxide (**7**) from (**5**) was 96% deduced from the yield of the propionyl complex (55%) and the good overall mass balance of the reaction. ^{1}H N.m.r. analysis of recovered (**5**) indicated a small amount of α-epimerisation had occured consistent with competing enolisation being responsible for the lack of complete conversion to sulphoxide (**7**). Optical rotation measurements showed recovered (*R*)-(**2**) and sulphoxide (**7**){$[\alpha]_D$ +181.0° (*c* 9.42, EtOH); lit.[8] $[\alpha]_D$ +171.1° (*c* 5.14, EtOH)} to be enantiomerically pure. ^{1}H N.m.r. analysis of (+)-sulphoxide (**7**) and its racemate in the presence of the chiral shift reagent described above confirmed the optical purity of (+)-(**7**). Since (*RSS*)-(**5**) produces (+)-sulphoxide (**7**) of known (*R*) absolute configuration the displacement reaction at sulphur has proceeded as expected with clean inversion of configuration.[9] Comparable results have been obtained using recovered (**5**) as starting material and with t-butyl and ethyl lithium dialkylcuprates.

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† The iron acetyl complex $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COMe]$ is available either as a racemate or enantiomerically pure (*S*)-(+) and (*R*)-(−) forms from B.P. Chemicals Ltd., New Specialities Business, Belgrave House, 76 Buckingham Palace Road, London SW1W 0SU, U.K.

‡ All new compounds gave satisfactory microanalytical and spectroscopic data.