Tetrahedron: Asymmetry Vol. 4, No. 7, pp. 1479-1480, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Resolution of the Chiral Iron Acetyl Complex [$(C_5H_5)Fe(CO)(PPh_3)COCH_3$]

Robert W. Baker and Stephen G. Davies*

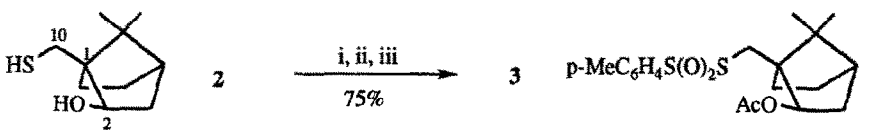
The Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, UK

(*Received in UK* 12 *May* 1993)

Abstract: Reaction of the lithium enolate of racemic iron acetyl complex [$(C_5H_5)Fe(CO)(PPh_3)COCH_3$] with the thiolsulphonate **3**, derived from homochiral (1*S*)-10-mercaptoisoborneol **2**, provides the diastereomeric α-sulphides **4** and **5**. Selective oxidation of diastereomer **4** to the sulphoxide **6** ($k_{ox.4}$ / $k_{ox.5}$ = *ca.* 20-25) allows facile separation from the sulphide **5**. Subsequent desulphurisation of **6** and **5** furnishes the homochiral (*R*)-(-)- and (*S*)-(+)-acetyl complexes in overall yields (maximum 50%) of 21% and 27% respectively from the racemate.

The iron chiral auxiliary [$(C_5H_5)Fe(CO)(PPh_3)$] exerts powerful stereochemical control over a wide variety of reactions associated with attached acyl ligands.[1] The literature procedure[2] for the preparation of the parent acetyl complex **1** in homochiral (enantiomerically pure) form provides only very limited access to (*R*)-(-)-**1** and (*S*)-(+)-**1**.[3] We report herein a novel resolution procedure for the preparation of homochiral **1**.

We have previously demonstrated the completely stereoselective oxidation of (*R,S*)-[$(C_5H_5)Fe(CO)(PPh_3)COCHMeSPh$] to the corresponding (*R,S,S*)-sulphoxide with *m*-chloroperbenzoic acid (*m*-CPBA) at -100°C.[4] The oxidation with *m*-CPBA of sulphides derived from (1*S*)-10-mercaptoisoborneol **2** has also been shown to proceed with good stereoselectivity (≥9:1).[5] It was therefore anticipated that resolution of the racemic acetyl complex **1** might be effected through selective oxidation of one of the two diastereomeric α-sulphides derived from homochiral **2**; for this diastereomer the stereocontrol exerted by the iron centre would complement that exerted by the isoborneol moiety. Both the thiol and hydroxyl groups of **2** were acetylated, the acetylthio group converted to the sulphenyl chloride with sulphuryl chloride, and the sulphenyl chloride then treated with the sodium salt of *p*-toluenesulphinic acid to give the thiolsulphonate **3** {$[\alpha]_D^{22}$ = - 8.6 (*c* 0.65, toluene)} in 75% overall yield from **2** (Scheme 1).

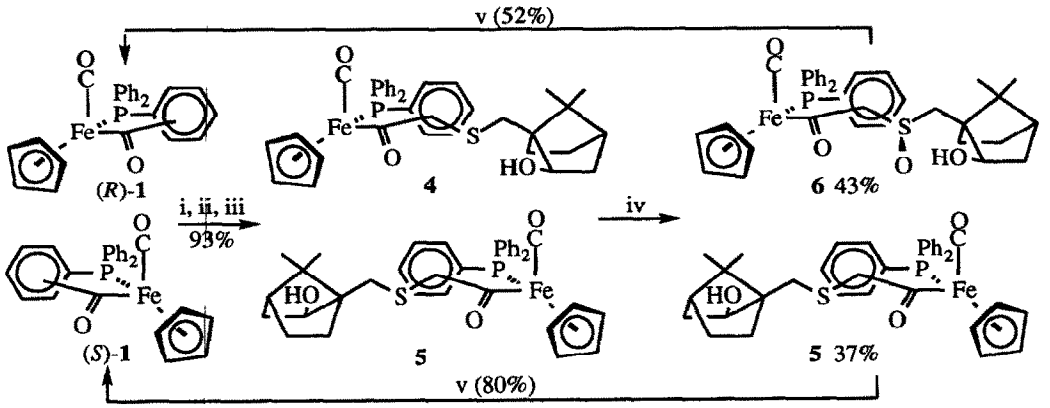


Scheme 1. *Reagents and Conditions:* i, Ac_2O, pyridine, DMAP, CH_2Cl_2; ii, SO_2Cl_2, heptane; iii, aqueous *p*-$MeC_6H_4S(O)_2Na$, heptane.

Reaction of the lithium enolate of the racemic acetyl complex **1** with **3**, followed by deacetylation, gave a chromatographically inseparable 1:1 mixture of the diastereomers **4** and **5** in 93% yield from **1** (quantitative when corrected for recovered racemic acetyl complex; Scheme 2). As expected, one of the diastereomers was found to undergo oxidation with *m*-CPBA at a considerably greater rate than the other. By monitoring the diastereomeric excess (d.e.) of the unreacted sulphide versus equivalents of *m*-CPBA it was possible to determine, using the equations developed for kinetic resolution,[6] that the rate of oxidation of **4** was *ca.* 20-25 times faster than the rate of oxidation of **5**. Thus, addition of 0.6 equivalents of *m*-CPBA to a tetrahydrofuran solution of the 1:1 mixture of **4** and **5** (-100°C, 2 hrs), followed by easy separation of sulphide from sulphoxide

over basic alumina ($\Delta R_f = 0.6$, 9:1 CH_2Cl_2/EtOAc), gave the sulphide **5** {$[\alpha]_D^{22} = -28.1$ (*c* 0.21, toluene)} in 37% isolated yield and in greater than 99% d.e. by ^1H n.m.r. analysis at 300 MHz. Desulphurisation of the sulphide **5** with nickel boride then gave (*S*)-(+)-**1** {$[\alpha]_{546}^{22} = +285$ (*c* 0.22, C_6H_6); lit.[7] $[\alpha]_{546}^{22} = +288$ (*c* 0.04, C_6H_6)} in 80% yield (27% overall from the racemate).[8]

Flash chromatography of the sulphoxide mixture and recrystallisation gave **6** {$[\alpha]_D^{22} = -26.4$ (*c* 0.28, toluene)} in 43% yield and with a ≥98% d.e. Although the stereochemistry assigned to **6** at the sulphur centre has not been unambiguously determined, it's assignment is consistent with the stereoselectivity previously observed for the *m*-CPBA oxidation of both (*R,S*)-[$(C_5H_5)Fe(CO)(PPh_3)COCHMeSPh$][4] and for sulphides derived from **2**.[5] Desulphurisation of the sulphoxide **6** with nickel boride furnished (*R*)-(-)-**1** {$[\alpha]_{546}^{22} = -284$ (*c* 0.21, C_6H_6)} in 52% yield (21% overall from the racemate).[8]



Scheme 2. *Reagents and Conditions:* i, butyllithium, THF, -78°C; ii, inverse addition to **3** (1.2 equivalents), THF, -78°C; iii, NaOMe, MeOH, THF, 60°C; iv, *m*-CPBA (0.6 equivalents), THF, -100°C; v, $NiCl_2$ (10 equivalents), $NaBH_4$ (25 equivalents), EtOH, THF, -15°C.

The overall yields for the resolution represent a significant improvement over those reported in the literature.[2] Additionally, the ease of the chromatographic separations involved in the procedure readily allows access to homochiral **1** in multigram quantities.

We thank BP International Ltd. for a Venture Research Award.

References

1. S.G. Davies, *Aldrichimica Acta*, 1990, **23**, 31.
2. H. Brunner and E. Schmidt, *J. Organomet. Chem.*, 1972, **36**, C18; H. Brunner and E. Schmidt, *ibid.*, 1973, **50**, 219; H. Brunner and J. Strutz, *Z. Naturforsch., Teil B*, 1974, **29**, 446.
3. (*R*)-(-)-**1** and (*S*)-(+)-**1** are available from Oxford Asymmetry Ltd.,57 Milton Park, Abingdon, Oxon OX14 4RX, U.K.
4. S.G. Davies and G.L. Gravatt, *J. Chem. Soc., Chem. Commun.*, 1988, 780.
5. O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle and G. Modena, *J. Org. Chem.*, 1986, **51**, 1457.; R. Annunziata, M. Cinquini, F. Cozzi, S. Farina and V. Montanari, *Tetrahedron*, 1987, **43**, 1013; B.M. Eschler, R.K. Haynes, S. Kremmydas and D.D. Ridley, *J. Chem. Soc., Chem.Commun.*, 1988, 137; Y. Arai, K.Hayashi,T.Koizumi, M. Shiro and K. Kuriyama, *Tetrahedron Lett.*, 1988, **29**, 6143.; S.G.Pyne, P. Bloem and R. Griffith, *Tetrahedron*, 1989, **45**, 7013; Y. Arai, K.Hayashi, M. Matsui, T.Koizumi, M. Shiro and K. Kuriyama, *J. Chem. Soc., Perkin Trans. I*, 1991, 1709.
6. H.B. Kagan and J.C. Fiaud, *Topics Stereochem.*, 1988, **18**, 249.
7. S.G. Davies, I.M. Dordor-Hedgecock, K.H. Sutton, J.C. Walker, C. Bourne, R.H. Jones and K. Prout, *J. Chem. Soc., Chem. Commun.*, 1986, 607.
8. The enantiomeric excess of the resolved complexes was confirmed as ≥98% by ^1H n.m.r. analysis in the presence of Eu(tfc)$_3$.[7]