Chiral Recognition in the Reaction of the Enolate derived from $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2OCH_2Ph]$ with 1-Phenylethyl Bromide

Stephen G. Davies,*[a] David Middlemiss,[b] Alan Naylor,[b] and Martin Wills[a]

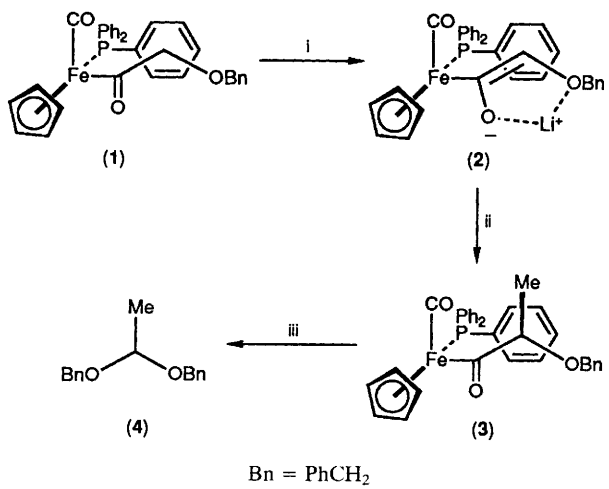
[a] *The Dyson Perrins Laboratory, South Parks Road, Oxford OX1 3QY, UK*
[b] *Glaxo Group Research, Ware, Herts. SG12 0DJ, UK*

Chiral recognition to the extent of 30 : 1 has been observed in the reaction between the homochiral iron acyl complex $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2OCH_2Ph]$ and racemic 1-phenylethyl bromide.

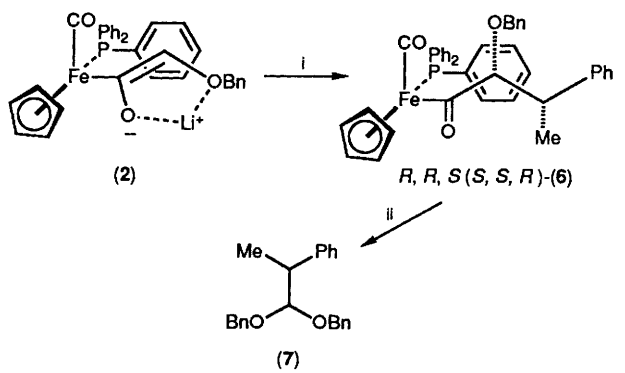
There are very few examples of nucleophiles which react selectively with one enantiomer of a racemic chiral electrophile.[1] Methodology of this type is especially attractive since both the recovered electrophile and the product may, in principle, be obtained in enantiomerically pure form. Alternatively, if the electrophile is subject to a racemisation process during the reaction, full conversion of a racemate to a homochiral product may be possible. In this paper a homochiral nucleophile is described which exhibits a high degree of chiral recognition in its reaction with 1-phenylethyl bromide.

Deprotonation of the racemic α-benzyloxy iron acyl complex (**1**) using butyl-lithium in tetrahydrofuran (THF) results in the formation of a deep red solution of the *E* enolate (**2**), the geometry of which is determined by co-ordination of the oxygen atoms to the lithium cation prior to deprotonation. Addition of methyl iodide to this enolate gives the diastereoisomerically pure complex *R,R*(*S,S*)-(**3**), the result of electrophile addition to the face of the enolate away from the bulky triphenylphosphine ligand when it lies in the *anti* (O⁻ to CO) conformation.[2] Oxidative decomplexation of (**3**) using bromine in the presence of benzyl alcohol gives the dibenzyl acetal (**4**), a product which results from the unusual cleavage of the C_{acyl}–C_α bond, assisted by electron donation from the ether oxygen atom.[3] This sequence of reactions (Scheme 1) illustrates the application of the complex (**1**) as a formyl anion equivalent.

Addition of racemic 1-phenylethyl bromide (**5**) to the racemic enolate (**2**) (−40 °C, 10 h) led to the formation of diastereoisomerically pure complex (**6**) in 83% yield. This result indicates that a chiral recognition interaction had occurred between the two reagents such that a given enan-



Scheme 1. *Reagents and conditions*: i, Bu^{n}Li, THF, −78 °C; ii, MeI, −78 °C; iii, Br_2, BnOH, CH_2Cl_2, −78 °C.



Scheme 2. *Reagents and conditions*: i, (±)-PhMeCHBr (**5**), THF, −78 °C, 10 h; ii, Br_2, BnOH, CH_2Cl_2, −78 °C.

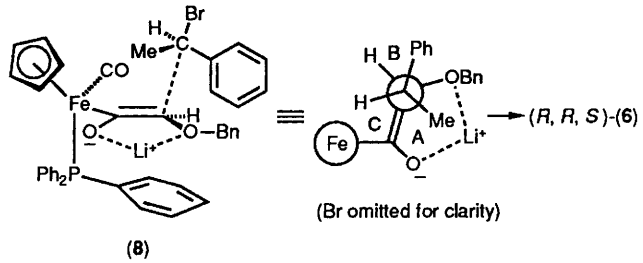


Figure 1. Reaction of the *R* enolate with (*R*)-1-phenylethyl bromide.

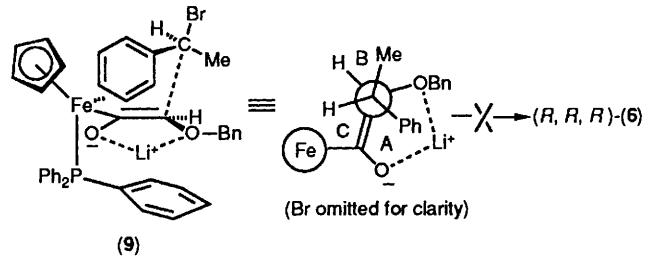
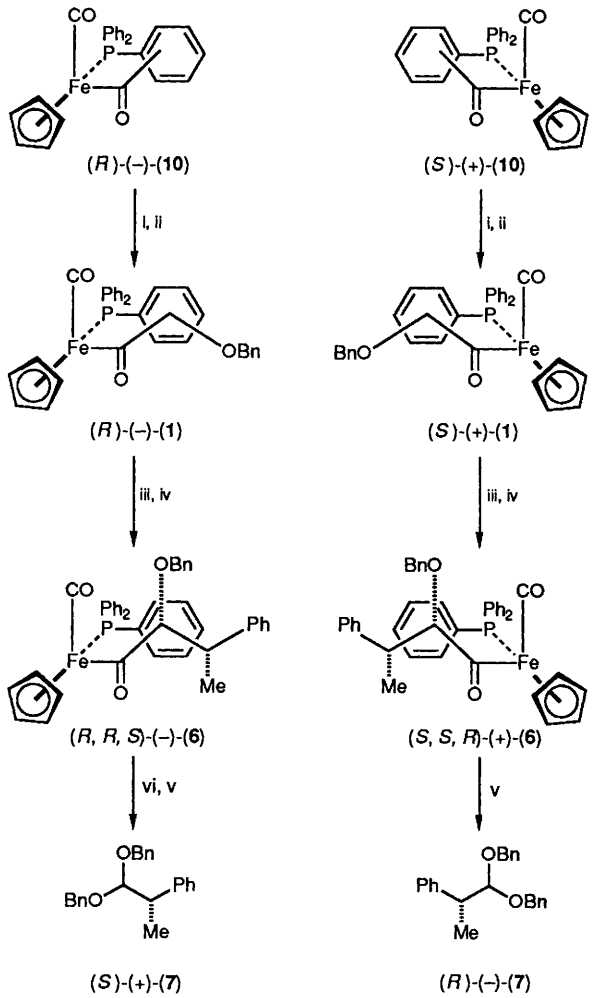


Figure 2. Reaction of the *R* enolate with (*S*)-1-phenylethyl bromide.

tiomer of the iron enolate had reacted with only one enantiomer of the alkyl halide. Inspection of molecular models (discussed below) suggested that the best matched pair would involve the reaction of the enolate of *R* configuration with the alkyl halide of *R* configuration (and therefore *S* enolate with *S* alkyl halide). This was confirmed by an *X*-ray crystal structure analysis of (**6**) which unambiguously established the configurations as *R,R,S*(*S,S,R*). Oxidative decomplexation of (**6**) in the presence of benzyl alcohol gave the dibenzyl acetal (**7**) in 85% yield.

The remarkable chiral recognition observed in this reaction results from the well defined nature of the enolate and the arrangement of the surrounding ligands. The source of the high stereoselectivity of α-alkylation has been discussed above. If it is assumed that the 1-phenylethyl bromide approaches the enolate such that its substituents at the carbon attached to the bromine atom are staggered with respect to those at the enolate α-centre then only the smallest group on the halide may occupy the sterically demanding region C as depicted in Figures 1 and 2, owing to its proximity to the bulky cyclopentadienyl ring. It is therefore necessary that the reaction between enolate (**2**) of *R* configuration and alkyl halide of *R* configuration proceeds *via* transition state (**8**) (Figure 1) and that between *R* enolate and *S* halide *via* transition state (**9**) (Figure 2). A comparison of transition states (**8**) with (**9**) reveals that in the former there are two steric *gauche* interactions of the methyl group of the alkyl halide and only one such interaction of the phenyl group with substituents on the enolate (*gauche* interactions involving protons are not considered to affect the reaction). In the latter transition state (**9**), however, there are two *gauche* interactions involving the phenyl and only one involving the methyl group. Since *gauche* interactions involving the phenyl ring are likely to outweigh those involving the methyl group, transition state (**8**) would be predicted to lead to the major product, which is in agreement with the experimental result. In addition, since the lowest energy transition states are expected



Scheme 3. *Reagents and conditions*: i, Bu^{n}Li, THF, −78 °C, 1 h, then MoOPH, THF, −40 °C, 4 h; ii, BnBr, NaH, THF, 20 °C, 12 h; iii, Bu^{n}Li, THF, −78 °C, 1 h; iv, (±)-PhMeCHBr (2 equiv.), THF, −40 °C, 10 h; v, Br_2, BnOH, CH_2Cl_2, −78 °C; vi, recrystallisation from dichloromethane/hexane.

to be those with the plane of the phenyl ring orthogonal to the carbon–bromine bond, transition state (**9**) involves interaction of the phenyl ring with the cyclopentadienyl ligand while this destabilising influence is absent in transition state (**8**).

The enantiomerically pure iron acyl complexes (*R*)-(−)-(**1**) and (*S*)-(+)-(**1**) were prepared by oxidation of the enolate derived from the commercially available homochiral acetyl complexes (*R*)-(−)- and (*S*)-(+)-(**10**)† using 'MoOPH'[4] followed by *O*-benzylation. Reaction of the enolate derived from (*S*)-(+)-(**1**) with two equivalents of racemic 1-phenylethyl bromide gave the diastereoisomeric products (*S,S,R*)- and (*S,S,S*)-(+)-(**6**) in a 30 : 1 ratio (71%). The selectivity is lower than for the racemic example because of the mass action effect, *i.e.*, as the reaction proceeds, the halide is depleted of the *S* enantiomer and the increase in the relative concentration of the *R* alkyl halide favours formation of the minor diastereoisomer. Although the halide was recovered in racemic form at the end of the reaction, it is likely that at −40 °C, the rate of the racemisation reaction (*via* a series of

† Homochiral complexes (*R*)-(−)-(**10**) and (*S*)-(−)-(**10**) are available from Oxford Chirality, PO Box 412, Oxford OX1 3QW, UK.

bromide promoted inversions)[5] is slow compared with that of the alkylation.[1c] Decomplexation of the 30:1 mixture of diastereoisomers (*S,S,R*)- and (*S,S,S*)-(+)-(**6**) gave (*R*)-(−)-(**7**) in 94% enantiomeric excess (e.e.) and 74% yield. The enantiomeric purity was assessed by the use of the ^{1}H NMR chiral shift reagent (*R*)-(−)-2,2,2-(trifluoromethyl)-9-anthryl ethanol[6] which provided baseline resolution of the separated benzylic signals from each enantiomer of racemic (**7**), but showed the presence of the two sets of peaks in a 30:1 ratio in the ^{1}H NMR spectrum of the enantiomerically enriched material from the latter reaction.

Reaction of (*R*)-(−)-(**1**) with two equivalents of racemic 1-phenylethyl bromide gave a 30:1 mixture of (*R,R,S*)- and (*R,R,R*)-(−)-(**6**). However, a single recrystallisation from dichloromethane/hexane provided diastereoisomerically pure (*R,R,S*)-(−)-(**6**) [73% overall from (*R*)-(−)-(**1**)] as assessed by 300 MHz ^{1}H NMR spectroscopy. Decomplexation of (*R,R,S*)-(−)-(**6**) gave the homochiral dibenzyl acetal (*S*)-(+)-(**7**) (78%), whose enantiomeric purity was confirmed using the chiral shift reagent decribed above.

The effectiveness of the chiral iron acyl complex (**1**) as a homochiral formyl anion equivalent capable of chiral recognition reactions has been demonstrated.

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