Kinetic Resolution of the Chiral Iron Acetyl Complexes [Fe(CO)(η^5-C_5H_5)(L)$COCH_3$] [L = PPh_3, P(*p*-tolyl)$_3$] *via* Aldol Reactions with Camphor

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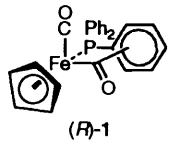
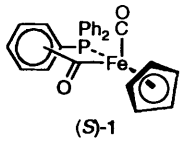
The chiral iron acetyl complexes [Fe(CO)(η^5-C_5H_5)(L)$COCH_3$] [L = PPh_3, P(*p*-tolyl)$_3$] have been kinetically resolved *via* aldol reactions involving their derived lithium enolates and camphor in the presence of lithium chloride. With (1*R*)-(+)-camphor the faster reacting iron acetyl enantiomer had the (*S*)-configuration allowing the (*R*)-iron acetyls to be obtained after recovery of starting material and crystallisation. The corresponding (*S*)-iron acetyls can be obtained by a base-promoted reverse aldol reaction of the isolated products. A mechanistic rationale for the high enantiomeric discrimination is proposed which involves a chelation-controlled chair transition state with a disfavourable 1-methyl to cyclopentadienyl interaction in the mismatched pairing.

The chiral iron acetyl complex [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCH_3$] **1** has been shown to be a versatile reagent for asymmetric synthesis with the iron chiral auxiliary [Fe(CO)(η^5-C_5H_5)(PPh_3)] exerting powerful control over a wide variety of reactions involving the acetyl and derived acyl moieties.[1] The key material in this area is the parent iron acetyl complex **1** and practical routes to the preparation of **1** in homochiral (enantiomerically pure) form are crucial for its development. The original procedures[2] for the preparation of homochiral **1** do not allow access to substantial amounts of material, therefore we have been investigating alternative methodologies.[3]

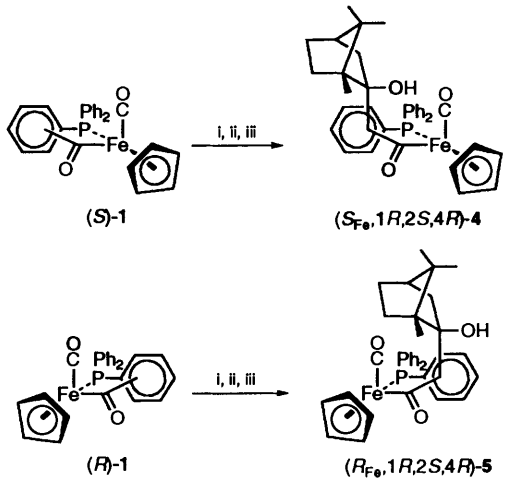

(*R*)-1


(*S*)-1

Enolates derived from the parent iron acetyl complex [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCH_3$] **1** have been shown to discriminate efficiently between the enantiotopic faces of the carbonyl functionality in aldehydes allowing highly stereoselective aldol reactions to be achieved.[4] We reasoned, therefore, that such enolates should show high enantiomeric discrimination on aldol addition to camphor **2**. In camphor **2** the faces of the carbonyl group are diastereotopic with only the *endo* face being accessible to nucleophiles, the *exo* face being blocked by the gem-dimethyl groups.[5]† Therefore, it seemed reasonable to expect matched and mismatched combinations between the enantiomers of **1** and the enantiomers of camphor **2** applicable to the kinetic resolution of racemic **1** with homochiral camphor. We describe herein the realisation of this for the kinetic resolution of the acetyl complex [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCH_3$] **1** and the extension of the methodology to the analogous complex [Fe(CO)(η^5-C_5H_5)(P(*p*-tolyl)$_3$)$COCH_3$][6] **3**. Part of this work has been previously communicated.[7]

Results

Treatment of the lithium enolate derived from the racemic iron acetyl complex (*RS*)-**1** and butyllithium at −78 °C with racemic (1*RS*)-(±)-**2** gave only one diastereoisomer (>100:1; 500 MHz ^{1}H NMR) of the aldol addition product ($S_{Fe}R_{Fe}$,1*RS*,2*SR*,4*RS*)-**4**[8]‡ (40% yield by ^{31}P NMR of the crude reaction mixture; 31% isolated) together with recovered iron acetyl complex **1** (60% by ^{31}P NMR of the crude reaction mixture). Under the same conditions homochiral (*S*)-**1** reacted with homochiral (1*R*)-(+)-camphor **2**§ to give the same diastereoisomer (S_{Fe},1*R*,2*S*,4*R*)-**4** (48% isolated yield) while little reaction was observed between homochiral (*R*)-**1** and (1*R*)-(+)-camphor **2** producing <5% of (R_{Fe},1*R*,2*S*,4*R*)-**5** (Scheme 1).



(*S*)-1 (S_{Fe},1*R*,2*S*,4*R*)-4
(*R*)-1 (R_{Fe},1*R*,2*S*,4*R*)-5

Scheme 1 *Reagents:* i, BuLi, THF, −78 °C; ii, (1*R*)-(+)-camphor **2**; iii, MeOH

Treatment of the racemic iron acyl complex (*RS*)-**1** with butyllithium (1.2 equiv.) at −78 °C generated a blood red solution of the lithium enolate. (1*R*)-(+)-Camphor **2** was added to the mixture which was then stirred at −78 °C for 90 min (Scheme 2). The starting material **1** (51%) and the aldol products (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** (41%) were

† The ability of the *syn* 7-methyl group of camphor to block the *exo* attack of nucleophiles is well documented.

‡ The stereochemical descriptors here refer to the IUPAC numbering system associated with the camphor carbon skeleton.

§ (1*R*)-(+)-camphor is the trivial name given to (1*R*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one.

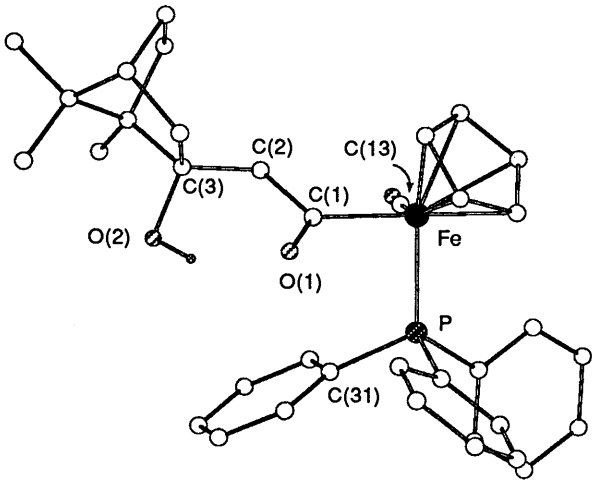


Fig. 1 X-ray crystal structure of (S_{Fe},1*R*,2*S*,4*R*)-**4**. Solvent of crystallisation ($CHCl_3$) has been omitted for clarity.

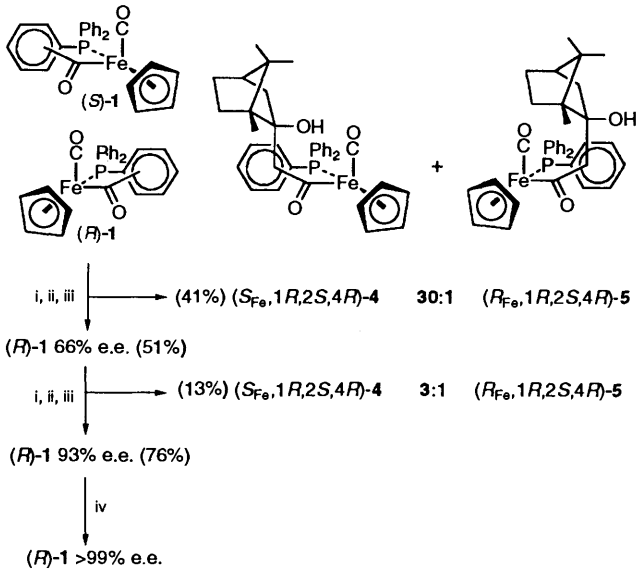
Table 1 Selected torsion and bond angles for (S_{Fe},1*R*,2*S*,4*R*)-**4** (°)

C(13)–Fe(1)–P(1)	93.1
C(1)–Fe(1)–P(1)	89.7
C(13)–Fe(1)–C(1)	93.6
C(1)–C(2)–C(3)–O(2)	−59.2
Fe(1)–C(1)–C(2)–C(3)	−171.7
C(1)–Fe(1)–P(1)–C(31)	30.7
O(1)–C(1)–C(2)–C(3)	4.2
O(1)–C(1)–Fe(1)–P(1)	55.8

separated with ease by flash chromatography on SiO_2. The enantiomeric excess of the recovered starting material **1** was determined to be 66% in favour of (*R*)-(−)-**1** by optical rotation, and this value was later confirmed by ^{1}H NMR spectroscopy using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol. The diastereoisomeric excess of the recovered aldol products **4** and **5** was determined to be 93% by integration of the resonances associated with the AB spin system of the α-methylene (FeCOCH_2) hydrogen atoms, which occur as a doublet of doublets centred at δ_4 3.29, 2.67 and δ_5 3.41, 2.80. The major diastereoisomer (S_{Fe},1*R*,2*S*,4*R*)-**4** was purified by crystallisation, and fully characterised. A single crystal X-ray analysis of (S_{Fe},1*R*,2*S*,4*R*)-**4** is shown in Fig. 1. Selected torsion and bond angles are presented in Table 1.

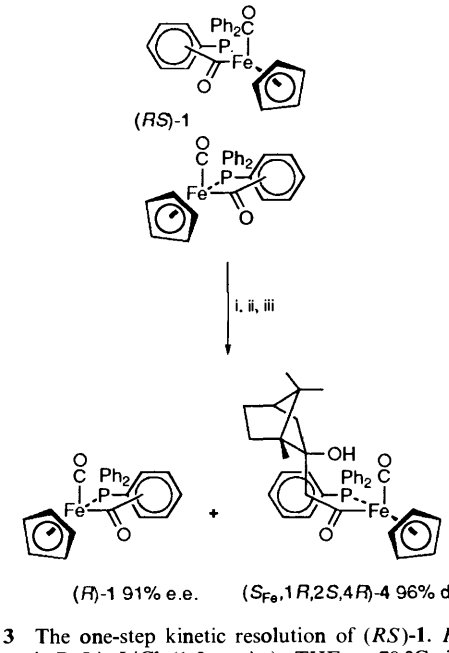
The enolate of the recovered, enantiomerically enriched starting material **1** (66% e.e.) was regenerated with butyllithium in tetrahydrofuran at −78 °C, and treated with (1*R*)-(+)-**2** at −78 °C (Scheme 2). Work-up and chromatography as before afforded a mixture of the two diastereoisomeric aldol products **4** and **5** (13%) (3:1 respectively by ^{1}H NMR; 50% d.e.), and starting material **1** (76%). The enantiomeric excess of the recovered iron acetyl complex (*R*)-(−)-**1** was determined to be 93% by optical rotation and chiral shift studies. After a single crystallisation from chloroform using light petroleum (b.p. 40–60 °C), (*R*)-(−)-**1** could be obtained in homochiral (>99% e.e.) form. Overall yields for the resolution depend upon the efficiency of this final crystallisation step, which varied from a minimum of 51% to a maximum of 93%. Thus, overall, 19–36% homochiral (*R*)-(−)-**1** {$[\alpha]_{546}^{25}$ −288 (*c* 0.04, C_6H_6)}[8] was obtained from the starting racemate (*RS*)-**1** (maximum 50% for a single enantiomer of the starting racemate), using (1*R*)-(+)-camphor **2** in a sequential kinetic resolution protocol. The enantiomeric purity of the recrystallised complex (*R*)-**1** was confirmed by ^{1}H NMR spectroscopy using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol.

The efficiency of the resolution methodology described above



Scheme 2 The sequential kinetic resolution of (*RS*)-**1**. *Reagents and conditions:* i, BuLi, THF, −78 °C; ii, (1*R*)-(+)-camphor **2**; iii, MeOH; iv, recrystallisation.

may be enhanced significantly by the addition of lithium chloride.[9] Thus, under optimal conditions, generation of the enolate (*RS*)-**1** with butyllithium in the presence of lithium chloride (1.5 equiv.), followed by treatment with (1*R*)-(+)-camphor **2**, affords (*R*)-**1** with an enantiomeric excess of 91% (Scheme 3). A single crystallisation from hexane–chloroform affords homochiral (*R*)-**1** in an overall yield of 20–35%. The aldol product (S_{Fe},1*R*,2*S*,4*R*)-**4**, is recovered from the reaction mixture in >96% d.e.



Scheme 3 The one-step kinetic resolution of (*RS*)-**1**. *Reagents and conditions:* i, BuLi, LiCl (1.5 equiv.), THF, −78 °C; ii, (1*R*)-(+)-camphor **2**; iii, MeOH.

Transmetallation of the lithium enolate (*RS*)-**1** by treatment with diethylaluminium chloride[4a] before addition of (1*R*)-(+)-**2**, afforded 40% yield of a mixture of the two diastereoisomeric products (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** in the ratio 5:4. Treatment of the aluminium enolate of homochiral (*R*)-**1**

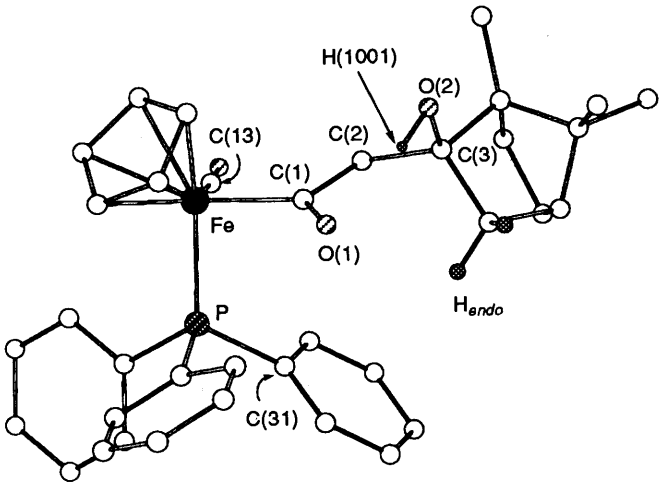
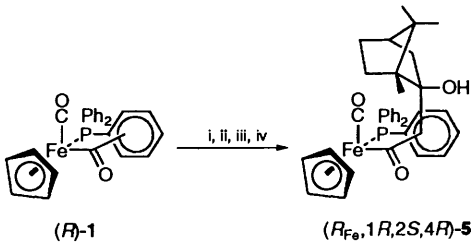


Fig. 2 X-ray crystal structure of (R_{Fe},1*R*,2*S*,4*R*)-**5**. Solvent of crystallisation [$CH_3CH(OH)CH_3$] and selected hydrogen atoms have been omitted for clarity.

Table 2 Selected torsion and bond angles for (R_{Fe},1*R*,2*S*,4*R*)-**5** (°)

C(13)–Fe(1)–P(1)	94.2
C(1)–Fe(1)–P(1)	91.2
C(13)–Fe(1)–C(1)	95.0
C(1)–C(2)–C(3)–O(2)	−55.0
Fe(1)–C(1)–C(2)–C(3)	167.9
C(1)–Fe(1)–P(1)–C(31)	−31.7
O(1)–C(1)–C(2)–C(3)	−6.4
O(1)–C(1)–Fe(1)–P(1)	−70.7

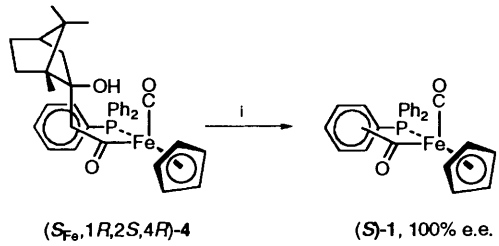
with (1*R*)-(+)-**2** gave, after work-up and chromatography, the single diastereoisomer (R_{Fe},1*R*,2*S*,4*R*)-**5** (31%) (Scheme 4), which was fully characterised. A single crystal X-ray analysis of (R_{Fe},1*R*,2*S*,4*R*)-**5** is shown in Fig. 2. Selected torsion and bond angles are presented in Table 2.



Scheme 4 The direct synthesis of (R_{Fe},1*R*,2*S*,4*R*)-**5**. *Reagents and conditions:* i, BuLi, THF, −78 °C; ii, Et_2AlCl, −40 °C; iii, (1*R*)-(+)-camphor **2**, −78 °C; iv, MeOH.

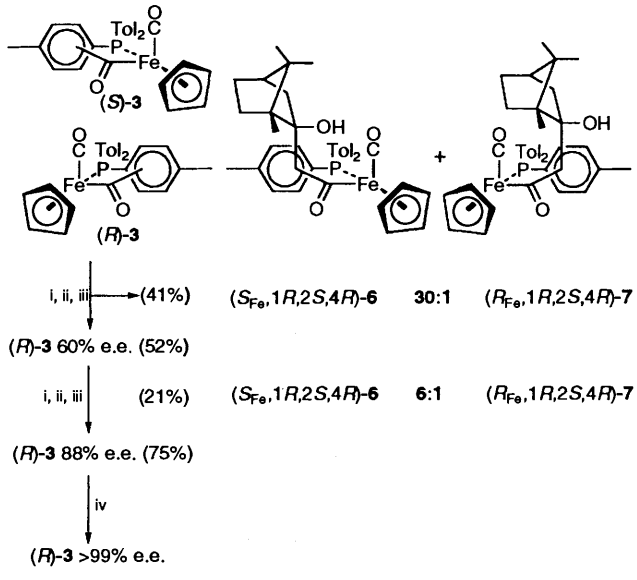
Treatment of a refluxing tetrahydrofuran solution of (S_{Fe},1*R*,2*S*,4*R*)-**4** with base (NaH, 3 equiv.) for 1.5 h, followed by methanol quench, afforded the iron acetyl complex (*S*)-**1** (Scheme 5). Alternatively, solid NaOMe (1 equiv.) may be used as the base, in which case the reaction mixture had to be heated at reflux for 6 h. Flash chromatography of the crude reaction mixture furnished (*S*)-(+)-**1** {$[\alpha]_{546}^{25}$ +288 (*c*. 0.04, C_6H_6)} [8] in 87% yield. The chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol, was used to establish that the recovered iron complex (*S*)-(−)-**1** was homochiral, thus indicating that racemisation of the iron stereogenic centre does not occur under these reaction conditions. The choice of base is important for the reaction to proceed to completion. For example, refluxing a tetrahydrofuran solution of **4** in the presence of 3 equiv. of LiH for 17 h, produces 9% of the acetyl complex (*S*)-**1**, as determined by ^1H NMR analysis of the crude reaction mixture, while an excess of KH resulted only in extensive decomposition.

Preliminary experiments indicated that in the presence of NaH in tetrahydrofuran at reflux (R_{Fe},1*R*,2*S*,4*R*)-**5** also generates the iron acetyl (*R*)-**1** efficiently.



Scheme 5 The synthesis of (*S*)-**1** from (S_{Fe},1*R*,2*S*,4*R*)-**4**. *Reagents and conditions:* i, NaH (1.5 h), or NaOMe (6 h), THF, heat.

Treatment of the lithium enolate derived from (*RS*)-[Fe(CO)(η^5-C_5H_5){P(*p*-tolyl)$_3$}$COCH_3$] **3** with (1*R*)-(+)-**2** at −78 °C generates, after work-up and chromatography, a mixture of diastereoisomeric aldol products (S_{Fe},1*R*,2*S*,4*R*)-**6** and (R_{Fe},1*R*,2*S*,4*R*)-**7** in a ratio of 30:1 respectively, and the iron acetyl complex (−)-**3** enriched with respect to the (*R*)-enantiomer (60% e.e.) (Scheme 6). Recrystallisation of the mixture of aldol products gave pure (S_{Fe},1*R*,2*S*,4*R*)-**6**, which was fully characterised. Repetition of the aldol reaction on the scalemic iron acetyl complex (*R*)-(−)-**3** (60% e.e.) furnished homochiral (*R*)-**3** after a single crystallisation (Scheme 6).



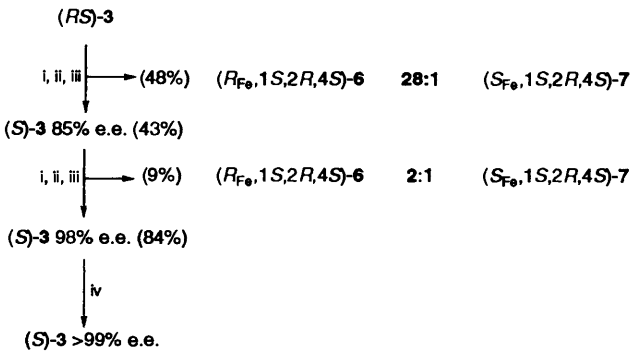
Scheme 6 The sequential kinetic resolution of (*RS*)-**3** into (*R*)-**3**. *Reagents and conditions:* i, BuLi, THF, −78 °C; ii, (1*R*)-(+)-camphor **2**; iii, MeOH; iv, recrystallisation.

The opposite enantiomer (*S*)-**3** may be produced from (*RS*)-**3** in a precisely analogous manner, this time using (1*S*)-(−)-**2** camphor (Scheme 7). The major diastereoisomer (R_{Fe},-1*S*,2*R*,4*S*)-**6**, the enantiomer of (S_{Fe},1*R*,2*S*,4*R*)-**6**, was isolated and fully characterised.

Treatment of the aluminium enolate derived from (*R*)-**3** with (1*R*)-(+)-**2** afforded after work-up and chromatography the single diastereoisomer (R_{Fe},1*R*,2*S*,4*R*)-**7** in 12% yield, which was fully characterised.

Discussion

In order to quantify whether any chiral discrimination could be expected between the enolate derived from **1** and camphor **2** the all-racemic reaction was investigated first. In the all-racemic



Scheme 7 The sequential kinetic resolution of (*RS*)-**3** into (*S*)-**3**. *Reagents and conditions:* i, BuLi, THF, −78 °C; ii, (1*S*)-(−)-camphor **2**; iii, MeOH; iv, recrystallisation.

case the ratio of product diastereoisomers correlates directly with the rate ratio for each iron acetyl enolate enantiomer reacting with the two camphor enantiomers and *vice versa*, since the effects of mass action are eliminated under these conditions. A very high discrimination (>100:1) between matched and mismatched pairs was found. The major aldol diastereoisomer was also formed as the only product from homochiral (*S*)-**1** and (1*R*)-(+)-camphor **2** and could, therefore, be assigned as ($S_{Fe}R_{Fe}$, 1*RS*,2*SR*,4*RS*)-**4** assuming only *endo* addition to camphor; the assignment was confirmed by a single-crystal X-ray structure analysis on (S_{Fe},1*R*,2*S*,4*R*)-**4**. This also identified the matched pairs as (*S*)-**1** and (1*R*)-(+)-camphor **2** and (*R*)-**1** and (1*S*)-(−)-camphor **2**. Recovery (44%) of the iron acetyl complex in the all racemic case was indicative of deprotonation of camphor by the enolate competing with the aldol reaction.

Although the very high enantiomeric discrimination in the aldol reaction should allow an efficient kinetic resolution procedure of racemic iron acetyl (*RS*)-**1** with homochiral camphor, the essentially non-stereoselective protonation of the enolate by camphor to regenerate racemic (*RS*)-**1** is deleterious. Thus, kinetic resolution of (*RS*)-**1** with homochiral (1*R*)-(+)-camphor **2** generated the aldol products (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** in the expected 30:1 ratio (lower than the all racemic case as a result of mass action) but recovered (*R*)-**1** only had an e.e. of 66%. Repetition of the kinetic resolution on the thus formed scalemic (*R*)-**1** gave material of sufficiently high e.e. to allow homochiral material to be obtained by a single recrystallisation (Scheme 2).

The presence of lithium chloride favours the aldol addition over the enolate protonation and hence enhances the efficiency of the kinetic resolution (Scheme 3) allowing, under optimal conditions, homochiral (*R*)-**1** to be obtained after a single aldol reaction with (1*R*)-(+)-camphor **2**.

All attempts to isolate and characterise the minor diastereoisomer (R_{Fe},1*R*,2*S*,4*R*)-**5** generated in the course of the reaction of the lithium enolate of (*RS*)-**1** with (1*R*)-(+)-**2** were unsuccessful. Furthermore, the synthesis of (R_{Fe},1*R*,2*S*,4*R*)-**5** by the reaction of the lithium enolate of (*R*)-**1** with (1*R*)-(+)-**2** was impractical, because of the low yield (<5%). The lithium enolate of **1** shows poor stereoselectivity in the aldol addition with aldehydes, which is in marked contrast to the excellent stereoselectivity generally observed for the corresponding diethylaluminium enolate of **1** in the aldol addition with a variety of aldehydes.[4] Surprisingly, however, the reaction of the diethylaluminium enolate of (*RS*)-**1** with (1*R*)-(+)-**2** is *less* selective than that of the corresponding lithium enolate, affording a mixture of the two diastereoisomeric products **4** and **5** (40%), in the ratio of 5:4, respectively. Reaction of the aluminium enolate from (*R*)-**1** with (1*R*)-(+)-**2** thus provided a viable route to the synthesis of (R_{Fe},1*R*,2*S*,4*R*)-**5** (Scheme 4).

The sequential resolution procedure was also applied to the production of (*R*)- and (*S*)-[Fe(CO)(η^5-C_5H_5)[P(*p*-tolyl)$_3$]-$COCH_3$] **3** from racemic (*RS*)-**3** with (1*R*)-(+)- and (1*S*)-(−)-camphor **2**, respectively (Schemes 6 and 7). The increased efficiency of the latter resolution compared to the others is attributed to an older sample of butyllithium being used which is assumed to contain more lithium salts relative to base present.

In order to gain information about the competing enolate protonation by camphor, a series of trapping and labelling experiments was performed. The lithium enolate derived from (*RS*)-**1** is very reactive towards the electrophile methyl iodide, producing the propionyl complex [Fe(CO)(η^5-C_5H_5)(PPh_3)-$COCH_2CH_3$], quantitatively within 5 min at −78 °C. Quenching the reaction mixture derived from the addition of (1*R*)-(+)-**2** to the lithium enolate of (*RS*)-**1** after 1.5 h with anhydrous methyl iodide, before quenching with methanol, produced only 5% of the propionyl complex. This result is consistent with essentially all of the enolate either undergoing the aldol reaction or being protonated by the camphor.

For the purpose of the labelling studies, the 3-isotopomers of **2**, namely (1*R*)-(+)-3,3-dideuterio- ($\delta_{D\text{-}exo}$ 2.33, $\delta_{D\text{-}endo}$ 1.83) and (1*R*)-(+)-3-*endo*-deuterio-camphor (δ_D 1.83), were prepared by a literature procedure.[10] Since the parent acetyl complex [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCH_3$]-**1** does not undergo H/D exchange in the presence of weak base[11] (*e.g.* NaOMe/CD_3OD), the trideuterioacetyl isotopomer (*RS*)-[Fe(CO)(η^5-C_5H_5)(PPh_3)$COCD_3$] **1** (δ_D 2.33) was prepared by a slight modification of a literature procedure from CD_3I.[12]

Initially, we endeavoured to establish that the lithium enolate of (*RS*)-**1** was indeed being quenched by one of the acidic 3-hydrogen atoms of **2**. Thus, treatment of the lithium enolate of (*RS*)-**1** with (1*R*)-(+)-3,3-dideuteriocamphor at −78 °C, followed by ^{2}H NMR analysis of the recovered starting material **1**, revealed the incorporation of deuterium at the acetyl carbon (δ_D 2.35). Since the *exo* face of camphor is considerably more hindered than the *endo* face, it seemed likely that the enolate of (*RS*)-**1** may be quenched by the *endo* hydrogen atom of **2**. Thus, the lithium enolate of (*RS*)-**1** was treated with (1*R*)-(+)-3-*endo*-deuteriocamphor **2** at −78 °C. Once more, ^{2}H NMR analysis of the recovered starting material revealed the incorporation of deuterium at the acetyl carbon. In order to establish unambiguously that the 3-H_{endo} was wholly responsible for the protonation of the enolate, the lithium enolate derived from (*RS*)-[Fe(CO)(η^5-C_5H_5)(PPh_3)$COCD_3$] **1** was treated with (1*R*)-(+)-3-*endo*-deuteriocamphor **2** at −78 °C, and the reaction mixture was quenched with [$^2H_4$]methanol. The hydrogen atoms associated with (*RS*)-**1** resonate at 2.34. ^{1}H NMR analysis of the recovered starting material established that no ^{1}H incorporation had occurred. It was thus concluded that the 3-H_{endo} of camphor was exclusively responsible for any enolate quenching process by the camphor.

The lithium enolate of (*RS*)-[Fe(CO)(η^5-C_5H_5)(PPh_3)-$COCD_3$] **1** was generated in the usual manner and allowed to react with (1*R*)-(+)-**2** at −78 °C for 90 min. After work-up ([$^2H_4$]methanol quench) and chromatography, the iron acetyl complex was recovered as a 4:1 mixture by NMR analysis of [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCD_3$] and [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCHD_2$] with an enantiomeric excess as determined by ^{1}H NMR using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol of 68%, within experimental error of the enantiomeric excess of the bulk recovered starting material in the non-deuteriated series.

The conclusion that may be drawn from the above trapping and labelling experiments is that the enolate derived from **1** either undergoes an aldol reaction with camphor or abstracts the 3-H_{endo} of camphor. Protonation of the enolate occurs both on carbon (20%) to regenerate the acetyl complex **1** directly

and on oxygen (80%) to generate the corresponding enol. Protic work-up converts the enol to the acetyl complex **1** with concomitant proton exchange between the enol and solvent, *i.e.* in the case of the *O*-deuterio-enol being quenched with methanol the deuterium is washed out.

The crystal structures for the diastereoisomeric complexes (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** are shown in Fig. 1 and Fig. 2, respectively. The stereochemistries are as expected, and confirm that *endo* attack by the enolate of **1** upon the carbonyl function of (1*R*)-(+)-**2** occurs. In both cases the geometry about the iron centre is pseudo-octahedral with the acyl oxygen *anti* to the carbon monoxide ligand as is to be expected for complexes derived from **1**.[13] It is interesting to note the presence of an intramolecular hydrogen bond between the hydrogen atom of the β-hydroxy group, and the acyl oxygen of the iron species, for both **4** and **5**. Importantly, the intramolecular hydrogen bond of **5** (2.018 Å) is significantly weaker than that observed in **4** (1.894 Å). The ^{1}H NMR spectrum of the diastereoisomer (R_{Fe},1*R*,2*S*,4*R*)-**5** [and (R_{Fe},1*R*,2*S*,4*R*)-**7**] exhibits a doublet at 0.29 ppm [(R_{Fe},1*R*,2*S*,4*R*)-**7** = 0.25 ppm], which has been assigned as the 3-H_{endo} of the camphor moiety on the basis of the crystal structure. Closer inspection of the crystal structure of **5** (Fig. 2) reveals that the 3-H_{endo} of the camphor moiety is within 3.3 Å of the centre of the face of an aromatic ring associated with the triphenylphosphine ligand. The corresponding hydrogen atom in the diastereoisomer **4** (and **6**) is distal to the triphenylphosphine ligand and, therefore, does not experience such anisotropic shielding. One might conclude, therefore, that in chloroform at least, compound **5** adopts a conformation similar to that adopted in the crystal.

Molecular modelling studies were carried out using the CHEM-X package,* which employs van der Waals and electrostatic interaction energy calculations upon conformations generated by simple rigid rotor rotations about appropriate single bonds. This methodology has proven highly successful in determining the relative energies of accessible conformations for a wide variety of iron acetyl complexes.[13] The study of models associated with the transition state, and intermediates *en route* to the diastereoisomers (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5**, proved a most useful qualitative method for identifying the control elements operating during this highly stereoselective aldol reaction. The essence of our findings may be communicated using modified versions of the crystal structures associated with (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5**, which are presented in Fig. 3 and Fig. 4, respectively. Specifically, the torsion angles about the acyl moieties of the crystal structures of **4** and **5** have been altered, giving O(1)–C(1)–C(2)–C(3) = +90°, and −90°, respectively. The O(2)H–O(1) hydrogen bond has been maintained such that the geometries of the six atoms O(1)–C(1)–C(2)–C(3)–O(2)H approximate to a chair conformation. This was achieved by changing the torsion angles C(1)–C(2)–C(3)–O(2) of **4** and **5** to −60° and +60°, respectively. It was envisaged that this would afford a reasonable model for the initial conformations formed in a chelation-controlled aldol reaction and thus point to those factors important for recognition. Such a conformation for the mismatched product **5** (Fig. 4) results in significant steric crowding between the 1-methyl group on the camphor-derived fragment and the cyclopentadienyl ligand, while that for the matched product exhibits no such destabilising interaction (Fig. 3).

The retro-aldol reaction of **4** to release homochiral (*S*)-**1** is both preparatively useful and mechanistically interesting.

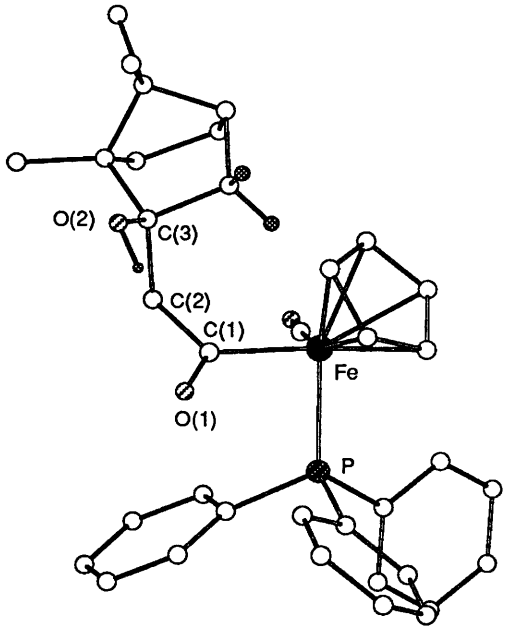


Fig. 3 Conformation generated from the X-ray structure of (S_{Fe},1*R*,2*S*,4*R*)-**4**. O(1)–C(1)–C(2)–C(3) = 90°, and C(1)–C(2)–C(3)–O(2) = −60°.

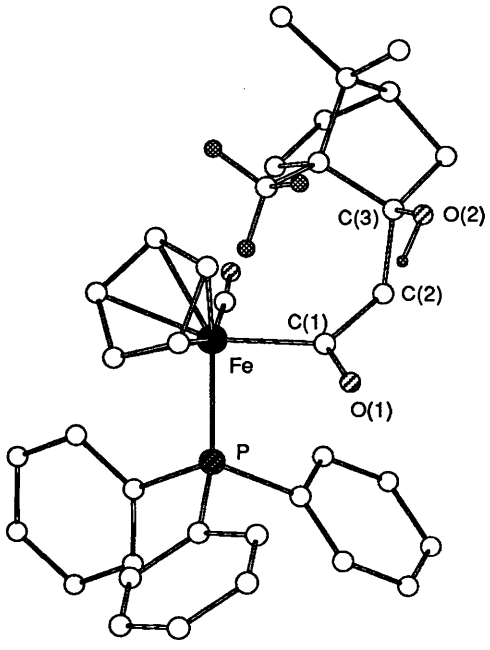


Fig. 4 Conformation generated from the X-ray structure of (R_{Fe},1*R*,2*S*,4*R*)-**5**. O(1)–C(1)–C(2)–C(3) = +90°, and C(1)–C(2)–C(3)–O(2) = 60°.

Compound **4** when heated alone in tetrahydrofuran at reflux for 16 h failed to produce any detectable amount of the acetyl complex **1**, whereas in the presence of base, presumably to form the corresponding sodium aldolate, the retro-aldol proceeded smoothly. The retro-aldol of the aldolate would initially produce the corresponding enolate, which is known to be unstable above *ca.* −30 °C, and camphor **2**. Since substantial amounts of the acetyl complex **1** are recovered in tetrahydrofuran, the initial enolate must be trapped rapidly by irreversible proton transfer from camphor **2**. Consistent with this proposal, performing the retro-aldol in tetrahydrofuran and subsequently adding methyl iodide to quench any enolate present produced no detectable amount of the propionyl

* CHEMX, designed and distributed by Chemical Design Limited, Roundway House, Cromwell House, Chipping Norton, Oxon OX7 5SR, UK.

complex, the acetyl complex **1** being isolated as before. In methanol the solvent would provide the proton quench.

Conclusions.—A viable kinetic resolution methodology has been established for the preparation of the homochiral iron acetyl complexes $[Fe(CO)(\eta^5\text{-}C_5H_5)(L)COCH_3]$[L = PPh_3 **1**, P(*p*-tolyl)$_3$ **3**]. Kinetic resolution of the derived lithium enolates in the presence of lithium chloride with (1*R*)-(+)-camphor yields the homochiral (*R*)-iron acetyl enantiomers. The (*S*)-iron acetyl enantiomers may be obtained by retro-aldol reaction of the products or by use of (1*S*)-(−)-camphor in the kinetic resolution procedure. Of the maximum of 50% yield for a single enantiomer, up to 36% has been achieved.

Experimental

General.—All reactions and purifications involving organometallic compounds were carried out under an atmosphere of nitrogen using vacuum-line and Schlenk-tube techniques. M.p.s are uncorrected. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Butyllithium was used as a 1.6 mol dm^{-3} solution in hexane, and diethylaluminium chloride was used at the specified concentration (1.8 or 2.0 mol dm^{-3}) in toluene. Camphor was sublimed immediately prior to use. All other reagents were used as received. Ether refers to diethyl ether. Flash chromatography was performed on silica (43–60 mm), and for organometallic complexes, under a positive nitrogen pressure. Light petroleum for column chromatography refers to the redistilled hydrocarbon fraction boiling in the range 40–60 °C. ^{1}H NMR spectra were recorded on either a Bruker WM-300 (300 MHz), or a Bruker AM-500 (500 MHz) spectrometer, using $CDCl_3$ as solvent and referenced to residual $CHCl_3$ with chemical shifts being reported as δ(ppm) from tetramethylsilane, and *J* values are measured in Hz. ^{13}C NMR spectra were recorded on a Bruker AM-250 spectrometer operating at 62.90 MHz using $CDCl_3$ as solvent and internal reference, and chemical shifts are reported as δ(ppm) from tetramethylsilane. ^{31}P NMR spectra were recorded on a Bruker AM-250 spectrometer operating at 101.26 MHz using $CDCl_3$ as solvent and chemical shifts are reported as δ(ppm) from an external reference of 85% orthophosphoric acid. ^{2}H NMR spectra were recorded on a Bruker AM-250 spectrometer operating at 38.4 MHz using $CHCl_3$ as solvent and $CHCl_3$ as internal reference. IR spectra were obtained as chloroform solutions in 1 mm cells on a Perkin-Elmer 297 instrument calibrated against polystyrene (1601 cm^{-1}) or using a Perkin-Elmer 1750 Infrared Fourier Transform Spectrometer. Mass spectra were recorded on a VG Micromass ZAB 1F instrument using field desorption techniques. Values for $[\alpha]_\lambda$ are given in units of 10^{-1} deg cm^2 g^{-1}. Elemental analyses were performed by the Dyson Perrins Laboratory Analytical Service. The complexes (*RS*)-**1** and (*RS*)-**3** were prepared according to literature methods.[1,2]

Determination of the Enantiomeric Purity of the Complexes **1** *and* **3** *by* ^{1}H *NMR Spectroscopy.*—A three-fold mass equivalent of the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol was added to a C_6D_6 solution of the iron acetyl complex **1** (or **3**) (5–7 mg). $\Delta\delta$ for the resonance arising from the acetyl methyl group is approximately 0.1 ppm (300 MHz). Under these conditions, the singlet associated with the methyl group of (*S*)-**1** [or (*S*)-**3**] resonates downfield (δ 2.5) of the corresponding signal arising from (*R*)-**1** [or (*R*)-**3**] (δ = 2.4).

($S_{Fe}R_{Fe}$,1RS,2RS,4RS)-*Carbonyl*(η-^{5}*cyclopentadienyl*)[(2-*hydroxy*-1,7,7-*trimethylbicyclo*[2.2.1]*heptan*-2-*yl*)*acetyl*](*triphenylphosphine*)*iron* **4**.—BuLi (1.7 cm^3, 2.63 mmol) was added to an orange solution of the acetyl complex (*RS*)-**1** (1.00 g, 2.19 mmol) in THF (15 cm^3) at −78 °C, and the resulting dark-red solution was stirred for 30 min. A solution of (1*RS*)-(±)-camphor-**2** (438 mg, 2.88 mmol) in THF (10 cm^3) was added dropwise to the mixture which was then stirred under N_2 at −78 °C for 90 min. The reaction was quenched with methanol, affording an orange solution which was allowed to warm slowly to room temperature. The THF and excess of methanol were removed under reduced pressure and an ether solution of the crude reaction mixture was filtered through a plug of silica. ^{1}H (500 MHz) and ^{31}P NMR analysis of the crude reaction mixture revealed a 3:2 mixture of starting material (*RS*)-**1** (δp 72.84) and ($S_{Fe}R_{Fe}$1*RS*,2*RS*,4*RS*)-**4** (δp 71.70) {present as a single diastereoisomer (>100:1)}, respectively. Column chromatography on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded in order of elution, (i) ($S_{Fe}R_{Fe}$,1*RS*,2*RS*,4*RS*)-**4** (409 mg, 31%) and (ii) (*RS*)-**1** (439 mg, 44%).

Kinetic Resolution of (RS)-*Acetyl*(*carbonyl*)(η-*cyclopentadienyl*)(*triphenylphosphine*)*iron* **1** *using* (1R)-(+)-*Camphor* **2**

Step A.—BuLi (8.3 cm^3, 13.3 mmol) was added to an orange solution of the acetyl complex (*RS*)-**1** (5.00 g, 11.01 mmol) in THF (40 cm^3) at −78 °C, and the resulting dark-red solution was stirred for 30 min. A solution of (1*R*)-(+)-camphor-**2** (2.18 g, 14.3 mmol) in THF (10 cm^3) was added dropwise to the mixture which was then stirred under N_2 at −78 °C for 90 min. The reaction was quenched with methanol, affording an orange solution which was allowed to warm slowly to room temperature. The THF and excess of methanol were removed under reduced pressure and an ether solution of the crude reaction mixture was filtered through a plug of silica. Column chromatography on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded in order of elution: (i) a mixture of the aldol products (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** (2.76 g, 41%) in a ratio of 30:1, respectively, as determined by ^{1}H NMR spectroscopy. This mixture was recrystallised from dichloromethane using hexane, affording (S_{Fe},1*R*,2*S*,4*R*)-**4** as a single diastereoisomer (Found: C, 71.3; H, 6.6. $C_{36}H_{39}FeO_3P$ requires C, 71.3; H, 6.5%); $[\alpha]_D^{25}$ −10.2 (*c* 0.53, $CHCl_3$); ν_{max}-(CH_2Cl_2)/cm^{-1} 3452 (OH), 1905 (Fe-C≡O) and 1750 (Fe-C=O); δ_H(500 MHz, $CDCl_3$) 0.59 (3 H, s, CH_3), 0.78 (3 H, s, CH_3), 0.88–0.95 (2 H, m), 1.04 (3 H, s, CH_3), 1.20–1.32 (3 H, m), 1.62–1.65 (1 H, m), 2.00–2.03 (1 H, m), 2.68 [1 H, d, J_{AB} 17, B of 'AB system', $CH_2C(O)Fe$], 3.28 [1 H, d, J_{AB} 17, A of 'AB system', $CH_2C(O)Fe$], 4.01 (1 H, s, OH), 4.43 (5 H, d, J_{PH} 1.2, C_5H_5) and 7.36–7.48 (15 H, m, PPh_3); δ_C(62.9 MHz, $CDCl_3$) 10.4, 20.9, 21.6 (CH_3), 27.0, 30.0 (CH_2), 45.3 (C-4), 47.8 (C-7), 48.4 (C-3), 51.8 (C-1), 73.3 [$CH_2C(O)Fe$], 79.9 (COH), 85.5 (C_5H_5), 128.3 (d, J_{PC} 9, PPh_3 C_{meta}), 130.0 (PPh_3 C_{para}), 133.4 (d, J_{PC} 9, PPh_3 C_{ortho}), 136.0 (d, J_{PC} 42, PPh_3 C_{ipso}), 220.1 (d, J_{PC} 25, FeC≡O) and 286.8 (d, J_{PC} 18, Fe*C*OCH_2); δ_P(101.2 MHz, $CDCl_3$) 71.70; *m*/*z* (FAB-MS) 383, 607 (M^+ + 1), and (ii) scalemic starting material $[Fe(CO)(\eta^5\text{-}C_5H_5)(PPh_3)COCH_3]$ **1** (2.56 g, 51%) $[\alpha]_{546}^{25}$ −188 (*c* 0.04, C_6H_6) which corresponds to 65% e.e. This value was confirmed by ^{1}H NMR using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol. Single crystals of **4**, suitable for X-ray analysis were grown from a concentrated solution of $CHCl_3$, layered with pentane.

Crystal Data for [R_{Fe},1R,2S,4R)-**4**·$CHCl_3$.—$C_{36}H_{39}FeO_3P$·$CHCl_3$, *M* = 725.9. Monoclinic, *a* = 17.205(5), *b* = 7.984(2), *c* = 13.635(3) Å, β = 109.86(2)°, *V* = 1762 Å^3 (by least squares refinement on the diffractometer angles for 24 automatically centred reflections, λ = 1.5418 Å), space group $P2_1$ (No. 4), *Z* = 2, D_x = 1.37 g cm^{-3}, *F*(000) = 756. Orange, rectangular needles. Crystal dimensions: 0.5 × 0.7 × 0.9 mm, μ(Cu-K$_\alpha$) = 63.02 cm^{-1}.

Data collection and processing. Enraf-Nonius CAD4 dif-

fractometer, $\omega/2\theta$ mode with ω scan width = 1.00 + 0.15 tan θ, ω scan speed = 1.3–5.9 deg min^{-1}, graphite-monochromated Cu-K_α radiation; 4878 reflections measured ($0 < \theta \leqslant 72°$, $-21 \leqslant h \leqslant 21$, $-1 \leqslant k \leqslant 9$, $-1 \leqslant l \leqslant 16$), 4248 unique [merging R = 0.047, after an empirical absorption correction (max., min. corrections = 0.722, 1.226)], giving 3488 with $I > 3\sigma(I)$. Three standard reflections measured every hour showed no appreciable decay.

Structure analysis and refinement. Direct methods[14] followed by full least-squares refinement,[15] anomalous dispersion correction applied, with all non-hydrogen atoms anisotropic and hydrogens in calculated positions, except hydroxy hydrogen H(2001) (observed difference map). The phenyl rings were regularised (*i.e.*, C–C distances of 1.390 Å and angles of 120°). The weighting scheme, a three-term Chebychev polynomial[16] (14.8, −5.83, 11.8), gave satisfactory agreement analyses. 372 Variables, observations/variables 9.4, $(\Delta\rho)_{max}$ = 0.70, $(\Delta\rho)_{min}$ = −0.40 e Å^{-3}. Flack enantiopole was refined to 0.01(1). Final R and R_w values were 0.047, 0.055, micro-Vax 3800 computer was used for all calculations.

Step B.—BuLi (4.2 cm^3, 6.72 mmol) was added to an orange solution of the recovered complex **1** (2.56 g, 5.64 mmol) in THF (15 cm^3) at −78 °C, and the resulting dark-red solution was stirred for 30 min. A solution of (1*R*)-(+)-**2** (1.12 g, 7.37 mmol) was added to the reaction mixture which was then stirred under N_2 at −78 °C for 90 min. The reaction was quenched with methanol, to give an orange solution which was allowed to warm slowly to room temperature. Removal of the THF and excess of methanol under reduced pressure gave a red oil. Chromatography on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded in order of elution, (i) a mixture of the aldol products (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** (540 mg, 13%) in the ratio of 3:1, respectively, and (ii) scalemic starting material **1** (1.95 g, 76%); $[\alpha]_{564}^{25}$ −268 (*c* 0.04, C_6H_6) which corresponds to 93% e.e. This was confirmed by ^{1}H NMR using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol. This fraction was recrystallised from dichloromethane with light petroleum to give homochiral (*R*)-**1** {lit.,[8] $[\alpha]_{564}^{25}$ −288 (*c* 0.04, C_6H_6)}. Yields for this procedure vary between a minimum of 51%, and a maximum of 93%, depending upon the efficiency of the crystallisation.

Kinetic Resolution of (RS)-*Acetyl(carbonyl)*-(η^5-*cyclopentadienyl*)(*triphenylphosphine*)*iron* **1** *in the Presence of* LiCl

Experiments were carried out using 0.5 (80%), 1.0 (63%), 1.5 (91%), 2.0 (74%) and 10.0 (65%) equivalents of LiCl. The highest enantiomeric excesses, for a given ratio of LiCl:(*RS*)-**1** are shown in parenthesis. The optimum conditions are associated with the addition of 1.5 equiv. of LiCl. In this instance, the enantiomeric excess of recovered **1** would vary between 80 and 91% e.e. The experimental details associated with the least selective example are as follows: BuLi (1.1 cm^3, 1.7 mmol) was added to a mixture of anhydrous lithium chloride (90 mg, 2.12 mmol) and the acetyl complex (*RS*)-**1** (643 mg, 1.42 mmol) in THF (15 cm^3) at −78 °C. The resulting dark-red solution was stirred for 30 min. A solution of (1*R*)-(+)-**2** (280 mg, 1.80 mmol) in THF (5 cm^3) was added dropwise to the mixture which was then stirred under N_2 at −78 °C for 90 min. The reaction was quenched using methanol, affording an orange solution which was allowed to warm slowly to room temperature. The THF and excess of methanol were removed under reduced pressure and a solution of the crude reaction mixture in ether was filtered through a plug of silica. Analysis of the crude reaction mixture by ^{31}P NMR revealed a 1:1 mixture of starting material and aldol product. Column chromatography on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded in order of elution, (i) the aldol products (S_{Fe},1*R*,2*S*,4*R*)-**4** and (R_{Fe},1*R*,2*S*,4*R*)-**5** (273 mg, 32%) >60:1, respectively, by 300 MHz ^{1}H NMR, and (ii) scalemic starting material [Fe(CO)(η^5-C_5H_5)(PPh_3)$COCH_3$] **1** (303 mg, 47%). An enantiomeric excess of 80% was determined by ^{1}H NMR studies using (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol.

(R_{Fe},1R,2S,4R)-*Carbonyl*(η^5-*cyclopentadienyl*)[(2-*hydroxy*-1,7,7-*trimethylbicyclo*[2.2.1]*heptan*-2-*yl*)*acetyl*](*triphenylphosphine*)*iron* **5**.—BuLi (2.1 cm^3, 3.36 mmol) was added to an orange solution of homochiral iron acetyl (*R*)-**1** (1.27 g, 2.80 mmol) in THF (15 cm^3) at −78 °C, and the resulting dark-red solution was stirred for 30 min. Diethylaluminium chloride (2 mol dm^{-3}; 4.2 cm^3, 8.4 mmol) was added to the reaction mixture, which was then warmed to −40 °C and stirred for 45 min. The mixture was re-cooled to −78 °C, and a solution of (1*R*)-(+)-**2** (0.55 g, 3.64 mmol) in THF (5 cm^3) was added to it; the reaction mixture was then stirred at −78 °C for 90 min. The reaction was quenched using methanol, and the resulting orange solution was allowed to warm slowly to room temperature. The THF and excess of methanol were removed under reduced pressure and a solution of the crude reaction mixture in ether was filtered through silica. Chromatography on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded in order of elution: (i) the aldol product (R_{Fe},1*R*,2*S*,4*R*)-**5** (0.535 g, 31%) (Found: C, 71.3; H, 6.1. $C_{36}H_{39}FeO_3P$ requires C, 71.3; H, 6.5%); $[\alpha]_{546}^{25}$ −89.8 (*c* 0.04, C_6H_6); $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3452 (OH), 1918 (Fe-C≡O) and 1592 (Fe-C=O); δ_H(500 MHz, $CDCl_3$) 0.29 (1 H, d, *J* 13, 3-H_{endo}), 0.55–0.65 (1 H, m), 0.76 (3 H, s, CH_3), 0.80 (3 H, s, CH_3), 1.03 (3 H, s, CH_3), 1.21–1.32 (2 H, m), 1.42–1.46 (1 H, m), 1.48–1.65 (2 H, m), 2.81 [1 H, d, J_{AB} 17, B of 'AB system', $CH_2C(O)Fe$], 3.41 [1 H, d, J_{AB} 17, A of 'AB system', $CH_2C(O)Fe$], 3.72 (1 H, s, OH), 4.41 (5 H, d, J_{PH} 1.2, C_5H_5) and 7.35–7.49 (15 H, m, PPh_3); δ_C(63 MHz, $CDCl_3$) 10.8, 20.9, 21.5 (CH_3), 26.5, 30.2 (CH_2), 45.2 (C-4), 46.5 (C-7), 48.7 (C-3), 51.9 (C-7), 74.8 [$CH_2C(O)Fe$], 80.1 (COH), 85.5 (C_5H_5), 129.0 (d, J_{PC} 9, PPh_3 C_{meta}), 129.8 (PPh_3 C_{para}), 133.3 (d, J_{PC} 9, PPh_3 C_{ortho}), 136.5 (d, J_{PC} 42, PPh_3 C_{ipso}), 220.2 (d, J_{PC} 30, FeC≡O) and 284.0 (d, J_{PC} 22, Fe*C*OCH_2); δ_P(101.2 MHz, $CDCl_3$) 71.97; *m/z* (FAB-MS) 383, 607 (M^+ + 1); and (ii) starting material (*R*)-[Fe(CO)(η^5-C_5H_5)(PPh_3)$COCH_3$] **1** (0.629 g, 49%). Single crystals of **5**, suitable for X-ray analysis were grown from a concentrated solution of $CHCl_3$, layered with propan-2-ol.

Crystal Data for (R_{Fe},1R,2S,4R)-**5**·Pr^{i}OH.—$C_{36}H_{39}FeO_3P{\cdot}C_3H_8O$, M = 666.6. Orthorhombic, a = 11.113(1), b = 11.820(1), c = 26.314(3) Å^3, V = 3456 Å^3 (by least squares refinement on the diffractometer angles for 24 automatically centred reflections, λ = 1.5418 Å), space group $P2_12_12_1$ (No. 19), Z = 4, D_x = 1.28 g cm^{-3}, F(000) = 1416. Orange, air-sensitive rectangular prisms. Crystal dimensions: 0.5 × 0.7 × 0.6 mm, μ(Cu-K_α) = 42.46 cm^{-1}.

Data collection and processing. Enras-Nonius CAD4 diffractometer, $\omega/2\theta$ mode with ω scan width = 1.00 + 0.15 tan θ, ω scan speed = 1.3–5.9 deg min^{-1}, graphite-monochromated Cu-K_α radiation; 4914 reflections measured ($0 < \theta \leqslant 50°$, $-1 \leqslant h \leqslant 11$, $-1 \leqslant k \leqslant 11$, $-1 \leqslant l \leqslant 26$), 4579 unique [merging R = 0.045, after an empirical absorption correction (max., min. correction = 0.537, 1.787)], giving 1940 with $I > 3\sigma(I)$. Three standard reflections measured every hour showed no appreciable decay.

Structure analysis and refinement. Direct methods[14] followed by full least-squares refinement,[15] anomalous dispersion correction applied, with all non-hydrogen atoms anisotropic and hydrogens in calculated positions, except hydroxy hydrogen H(1001) (observed difference map). The phenyl rings were

regularised (*i.e.*, C–C distances of 1.390 Å and angles of 120°) and group defined due to disorder in the solvent, constraints and restraints required: C–C bond distances restrained to 1.54(1) Å, C–O bond to 1.441(1) Å, all angles restrained to 109(1)° and all bonds restrained to have equal amplitudes of vibration along the bond. Unable to place accurately hydrogens in solvent due to disorder. The weighting scheme, a three-term Chebychev polynomial[16] (8.61, −3.03, 6.29), gave satisfactory agreement analyses. 255 Variables, observations/variables 7.6, $(\Delta\rho)_{max}$ = 1.13, $(\Delta\rho)_{min}$ = −0.64 e Å^{-3}. Flack enantiopole was refined to 0.00(1). Final R and R_w values were 0.067, 0.078, micro-Vax 3800 computer was used for all calculations.

Retro-aldol reaction of (S_{Fe},1*R*,2*S*,4*R*)-**4**. A solution of the aldol product (S_{Fe},1*R*,2*S*,4*R*)-**4** (3.56 g, 5.87 mmol), and NaH [(423 mg, 17.6 mmol), or NaOMe (1.05 equiv.)] were refluxed in THF (50 cm^3), under N_2 for 90 min (6 h in the case of NaOMe). The reaction mixture was allowed to cool to room temperature when MeOH was added to it to quench the excess of base. The orange solution was concentrated under reduced pressure, giving an orange solid. Flash chromatography of this on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded an orange solid which was characterised as (*S*)-[Fe(CO)(η^5-C_5H_5)-(PPh_3)$COCH_3$] **1** (2.345 g, 87%). ^{1}H NMR analysis using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol confirmed that racemisation had not occurred under the reaction conditions, and that the enantiomeric excess was >99%.

Kinetic Resolution of (RS)-*Acetyl(carbonyl)*-(η^5-*cyclopentadienyl*)(*tri*-p-*tolylphosphine*)*iron* **3** *using* (1R)- *and* (1S)-*Camphor*

With (1R)-(+)-*Camphor* **2**.—(*RS*)-**3** was resolved in a manner analogous to that described above for the resolution of (*RS*)-**1**. *Step A*. BuLi (0.9 cm^3, 1.38 mmol) was added to an orange solution of the acetyl complex (*RS*)-**3** (570 mg, 1.12 mmol) in THF (17 cm^3) at −78 °C, and the resulting dark-red solution was stirred for 30 min. A solution of (1*R*)-(+)-**2** (230 mg, 1.51 mmol) in THF (5 cm^3) was added dropwise to the mixture which was then stirred under N_2 at −78 °C for 90 min. The reaction was quenched with methanol, affording an orange solution which was allowed to warm slowly to room temperature. The THF and excess of methanol were removed under reduced pressure and a solution of the crude reaction mixture in ether was filtered through a plug of silica. Column chromatography on SiO_2 (EtOAc–light petroleum, 1:15 ⟶ 1:3 v/v) afforded in order of elution: (i) a mixture of the aldol products (S_{Fe},1*R*,2*S*,4*R*)-**6** and (R_{Fe},1*R*,2*S*,4*R*)-**7** in the ratio of 30:1, respectively, as determined by ^{1}H NMR. This mixture was recrystallised from ether using pentane, affording (S_{Fe},1*R*,-2*S*,4*R*)-*carbonyl*(η^5-*cyclopentadienyl*){(2-*hydroxy*-1,7,7-tri-*methylbicyclo*[2.2.1]*heptan*-2-*yl*)*acetyl*}(*tri*-p-*tolylphosphine*)-*iron* **6** as yellow microneedles (296 mg, 41%), m.p. 182–184 °C (Found: C, 72.4; H, 7.2; P, 4.7. $C_{39}H_{45}FeO_3P$ requires C, 72.2; H, 7.00; P, 4.8%); $[\alpha]_D^{25}$ −33 (*c* 0.53, CH_2Cl_2); ν_{max}(CH_2Cl_2)/cm^{-1} 3400 (OH), 1917 (Fe-C≡O) and 1586 (Fe-C=O); δ_H(500 MHz, $CDCl_3$) 0.57 (3 H, s, CH_3), 0.78 (3 H, s, CH_3), 0.89–0.95 (2 H, m), 1.04 (3 H, s, CH_3), 1.22–1.32 (2 H, m), 1.30 (1 H, d, *J* 13), 1.62–1.65 (1 H, m), 2.01 (1 H, br d, *J* 13), 2.37 (9 H, s, *p*-$C_6H_4CH_3$), 2.55 [1 H, d, J_{AB} 17, B of 'AB system', $CH_2C(O)Fe$], 3.25 [1 H, d, J_{AB} 17, A of 'AB system', $CH_2C(O)Fe$], 4.17 (1 H, s, OH), 4.43 (5 H, d, J_{PH} 1.2, C_5H_5), 7.17 (6 H, d, *J* 7, H_{meta} to P) and 7.34 (6 H, dd, J_{PH} 10.1, J_{HH} 8.6, H_{ortho} to P); δ_C(63 MHz, $CDCl_3$) 10.3, 20.9 (CH_3), 21.2 (*p*-$C_6H_4CH_3$), 21.6 (CH_3), 27.1, 30.1 (CH_2), 45.5 (C-4), 47.7 (C-7), 48.4 (C-3), 51.9 (C-1), 72.9 [$CH_2C(O)Fe$], 79.8 (COH), 85.5 (C_5H_5), 128.8 (d, J_{PC} 10, C_{meta} to P, *p*-$C_6H_4CH_3$), 132.8 (d, J_{PC} 45, C_{ipso} to P, *p*-$C_6H_4CH_3$), 133.2 (d, J_{PC} 9, C_{ortho} to P, *p*-$C_6H_4CH_3$), 139.8 (C_{ipso} to CH_3, *p*-$C_6H_4CH_3$), 220.2 (d, J_{PC} 30, FeC≡O) and 287.3 (d, J_{PC} 25, Fe*C*OCH_2); δ_P(101.2 MHz, $CDCl_3$) 68.73; *m/z* 649 (M^+ + 1), and (ii) scalemic **3** (0.30 g, 52%); $[\alpha]_D^{25}$ −83.8 (*c* 0.24, C_6H_6) which corresponds to 60% e.e.

Step B. Re-treatment of the recovered scalemic complex **3** (265 mg, 0.53 mmol) in THF (8 cm^3) with BuLi (0.40 cm^3, 0.64 mmol) at −78 °C followed by reaction with (1*R*)-(+)-**2** (110 mg, 0.72 mmol) in THF (3 cm^3) afforded after quenching and work-up as above, (i) a mixture of the aldol adducts **6** and **7** (73 mg, 21%) in a ratio of *ca.* 6:1 respectively by ^{1}H NMR; and (ii) scalemic **3** (200 mg, 75%) $[\alpha]_D^{25}$ −123 (*c* 0.20, C_6H_6) which corresponds to 88% e.e. This fraction was recrystallised twice from ether–pentane to give homochiral (*R*)-[Fe(CO)(η^5-C_5H_5)(P(*p*-tolyl)$_3$)$COCH_3$] as red microneedles (169 mg, 84%), m.p. 150–152 °C (Found: C, 70.0; H, 6.0; P, 6.0. $C_{29}H_{29}FeO_2P$ requires C, 70.2; H, 5.9; P, 6.2%); $[\alpha]_D^{25}$ −140 (*c* 0.24, C_6H_6). ^{1}H NMR studies, using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol confirmed that the e.e. was >99%.

With (1S)-(−)-*Camphor* **2**.—Racemic [Fe(CO)(η^5-C_5H_5)-(P(*p*-tolyl)$_3$)$COCH_3$] **3** was resolved in a manner precisely analogous to that described above. *Step A*. (RS)-**3** (2.74 g, 5.52 mmol) in THF (40 cm^3) was treated with BuLi (4.15 cm^3, 6.64 mmol) at −78 °C. Treatment with a THF (10 cm^3) solution of (1*S*)-(−)-**2** (1.09 g, 7.17 mmol), followed by methanol quench afforded, after concentration under reduced pressure, an orange–red residue. Column chromatography (SiO_2, EtOAc–petroleum) afforded, in order of elution, (i) a 28:1 mixture (^{1}H NMR, 500 MHz) of the aldol products (R_{Fe},1*S*,2*R*,4*S*)-**6** and (S_{Fe},1*S*,2*R*,4*S*)-**7** (1.72 g, 48%), respectively. This mixture was recrystallised from ether with pentane to give the aldol product (R_{Fe},1*S*,2*R*,4*S*)-**6**, the enantiomer of the previously described (S_{Fe},1*R*,2*S*,4*R*)-**6**, as yellow microneedles, m.p. 182–185 °C (Found: C, 72.4; H, 7.0; P, 4.7. $C_{39}H_{45}FeO_3P$ requires C, 72.2; H, 7.0; P, 4.8%); $[\alpha]_D^{25}$ +33.0 (*c* 0.26, C_6H_6), and (ii) scalemic **3** (1.19 g, 43%), $[\alpha]_D^{25}$ 119.6 (*c* 0.26, C_6H_6) which corresponds to 85% e.e.

Step B. Re-treatment of a THF (17 cm^3) solution of recovered scalemic **3** (1.12 g, 2.26 mmol) with BuLi (1.70 cm^3, 2.71 mmol) and a THF (5 cm^3) solution of (1*S*)-(−)-**2** (446 mg, 2.93 mmol), afforded after methanolic work-up and chromatography, (i) a 2:1 mixture of the aldol products (R_{Fe},1*S*,2*R*,4*S*)-**6** and (S_{Fe},1*S*,2*R*,4*S*)-**7** (130 mg, 9%), and (ii) **3** (940 mg, 84%), $[\alpha]_D^{25}$ +138.0 (*c* 0.27, C_6H_6), which corresponds to 98% e.e. This fraction was recrystallised from ether with pentane, affording red microneedles of homochiral (*S*)-[Fe(CO)(η^5-C_5H_5)(P(*p*-tolyl)$_3$)$COCH_3$] **3**, m.p. 158–160 °C (Found: C, 70.5; H, 5.7; P, 6.1. $C_{29}H_{29}FeO_2P$ requires C, 70.2; H, 5.9; P; 6.2%); $[\alpha]_D^{25}$ +140 (*c* 0.19, C_6H_6). ^{1}H NMR studies, using the chiral shift reagent (*S*)-(+)-1-(9-anthryl)-2,2,2-trifluoroethanol confirmed that the e.e. was >99%.

(R_{Fe},1R,2S,4R)-*Carbonyl*(η^5-*cyclopentadienyl*){(2-*hydroxy*-1,7,7-*trimethylbicyclo*[2.2.1]*heptan*-2-*yl*)*acetyl*}-(*tri*-p-*tolylphosphine*)*iron* **7**.—A solution of homochiral (*R*)-**3** (300 mg, 0.61 mmol) in THF (15 cm^3) was treated with BuLi (0.45 cm^3, 0.73 mmol) at −78 °C forming a deep burgundy red solution which was stirred for 30 min. The reaction mixture was then warmed to −42 °C and treated with diethylaluminium chloride (1.8 mol dm^{-3}; 1.02 cm^3, 1.81 mmol) forming a pale orange solution which was stirred for 2 h at −42 °C before being cooled to −78 °C. The reaction mixture was then treated with a solution of (1*R*)-(+)-**2** (120 mg, 0.79 mmol) and the mixture stirred for 2 h at −78 °C before being quenched with an excess of methanol. The reaction mixture was allowed to warm to room temperature, concentrated under reduced pressure and

purified by column chromatography on SiO_2 (EtOAc–petroleum, 1:15 ⟶ 1:3 v/v) to give in order of elution, (i) the aldol product **7** as a yellow solid (49 mg, 12%), which was recrystallised from ether–pentane as orange–red rods, m.p. 172–175 °C (Found: C, 71.9; H, 6.7. $C_{39}H_{45}FeO_3P$ requires C, 72.2; H, 7.0%); $[\alpha]_D^{25}$ −106.8 (*c* 0.56, CH_2Cl_2); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3452 (OH), 1915 (Fe-C≡O) and 1586 (Fe-C=O); δ_H(500 MHz, $CDCl_3$) 0.25 (1 H, d, *J* 13, 3-H_{endo}), 0.63–0.68 (1 H, m), 0.76 (3 H, s, Me), 0.80 (3 H, s, Me), 1.03 (3 H, s, Me), 1.20–1.27 (2 H, m), 1.41 (1 H, br t, *J* 4), 1.48–1.53 (1 H, m), 1.62 (1 H, br d, *J* 13), 2.36 (9 H, s, *p*-$C_6H_4CH_3$), 2.84 [1 H, d, J_{AB} 17, **B** of 'AB system', $CH_2C(O)Fe$], 3.30 [1 H, d, J_{AB} 17, **A** of 'AB system', $CH_2C(O)Fe$], 3.78 (1 H, s, OH), 4.39 (5 H, d, J_{PH} 1.2, C_5H_5), 7.18 (6 H, d, *J* 7, H_{meta} to P) and 7.38 (6 H, dd, J_{PH} 10, $J_{H_{ortho}H_{meta}}$ 8, H_{ortho} to P); δ_C(63 MHz, $CDCl_3$) 10.7, 20.9 (CH_3), 21.3 (*p*-$C_6H_4CH_3$), 21.5 (CH_3), 26.2, 30.2 (CH_2), 45.3 (C-4), 46.5 (C-7), 48.8 (C-3), 51.8 (C-1), 74.6 [$CH_2C(O)Fe$], 80.1 (COH), 85.5 (C_5H_5), 128.9 (d, J_{PC} 10, C_{meta} to P, *P*-$C_6H_4CH_3$), 132.8 (d, J_{PC} 45, C_{ipso} to P, *p*-$C_6H_4CH_3$), 133.3 (d, J_{PC} 9, C_{ortho} to P, *p*-$C_6H_4CH_3$), 139.8 (C_{ipso} to CH_3, *p*-$C_6H_4CH_3$), 220.6 (d, J_{PC} 30, FeC≡O) and 284.5 (d, J_{PC} 25, Fe*C*OCH_2); δ_P(102 MHz, $CDCl_3$) 68.99; *m*/*z* 649 (M^+ + 1) and, (ii) recovered starting material **5** (210 mg, 70%).

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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, *J. Organomet. Chem.*, 1973, **50**, 219; H. Brunner and J. Strutz, *Z. Naturforsch., Teil B*, 1974, **29**, 446.
3 R. W. Baker and S. G. Davies, *Tetrahedron Asymmetry*, 1993, **4**, 1479.
4 (*a*) S. G. Davies, I. M. Dordor-Hedgecock, P. Warner, R. H. Jones and K. Prout, *J. Organomet. Chem.*, 1985, **285**, 213; (*b*) S. C. Case-Green, S. G. Davies and C. J. R. Hedgecock, *Synlett*, 1991, **11**, 779; (*c*) L. S. Liebeskind, M. E. Welker and R. W. Fengl, *J. Am. Chem. Soc.*, 1986, **108**, 6328.
5 For example, see E. C. Ashby and J. T. Laemmle, *Chem. Rev.*, 1975, **75**, 527; J. R. Boone and E. C. Ashby, in *Topics in Stereochemistry*, eds. N. L. Allinger and E. L. Eliel, Interscience, New York, 1981, vol. **11**, ch. 2.
6 S. G. Davies, M. R. Metzler, K. Yanada and R. Yanada, submitted for publication.
7 S. C. Case-Green, J. F. Costello, S. G. Davies, N. Heaton, C. J. R. Hedgecock and J. C. Prime, *J. Chem. Soc., Chem. Commun.*, 1993, 1621.
8 S. G. Davies, I. M. Dordor-Hedgecock, R. J. C. Easton, S. C. Preston, K. H. Sutton and J. C. Walker, *Bull. Soc. Chim. Fr.*, 1987, 608.
9 The discovery that the addition of LiCl can effect the selectivity of reactions associated with lithium enolates is not new. For an excellent review, D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1624. For a recent example of the LiX effect, see B. J. Bunn and N. S. Simpkins, *J. Org. Chem.*, 1993, **58**, 533 and references cited therein.
10 J. W. Huffman and R. H. Wallace, *J. Am. Chem. Soc.*, 1989, **111**, 8691.
11 N. Aktogu, H. Felkin, G. S. Baird, S. G. Davies and O. Watts, *J. Organomet. Chem.*, 1984, **262**, 49.
12 M. Green and D. J. Westlake, *J. Chem. Soc. A*, 1971, 367.
13 S. G. Davies, A. E. Derome and J. P. McNally, *J. Am. Chem. Soc.*, 1991, **113**, 2854 and references therein.
14 G. M. Sheldrick, SHELXS User Guide, Institut für Anorganische Chemie der Universität, Göttingen, Germany.
15 D. J. Watkin, J. R. Caruthers and P. W. Betteridge, CRYSTALS User Guide. Chemical Crystallography Laboratory, University of Oxford (1985).
16 D. J. Watkin and J. R. Caruthers, *Acta Cryst., Sect. A*, 1979, **35**, 698.

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