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A Study of the Aldol Reaction between Enolates derived from the Iron Acetyl Complex [(η^5-C_5H_5)Fe(CO)(PPh3)COCH3] and 2,3-O-Isopropylidene-D-glyceraldehyde

Graham J. Bodwell, Stephen G. Davies* and Andrew A. Mortlock
The Dyson Perrins Laboratory, South Parks Road, Oxford, OX1 3QY, U.K.

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Abstract: Diethylaluminium enolates derived from the iron acetyl complex [(η^5-C_5H_5)Fe(CO)(PPh3)COCH3] undergo highly diastereoselective aldol reactions with the homochiral aldehyde, 2,3-O-isopropylidene-D-glyceraldehyde with the matched and mismatched pair reactions being readily identified. In both these reactions the observed diastereoselectivities may be rationalised in terms of the Masamune model for double asymmetric induction. Similarly the tin (II) enolates react in a predictable way, showing complementary diastereoselectivity, although effects attributed to enolate aggregation may suppress the mismatched pair reaction. However, the Masamune model cannot predict the results obtained with lithium enolates, where addition to the electrophile may occur under either chelation or non-chelation control. In the former case, both reagents reverse their selectivities as the initial two control elements are not mutually accommodating.

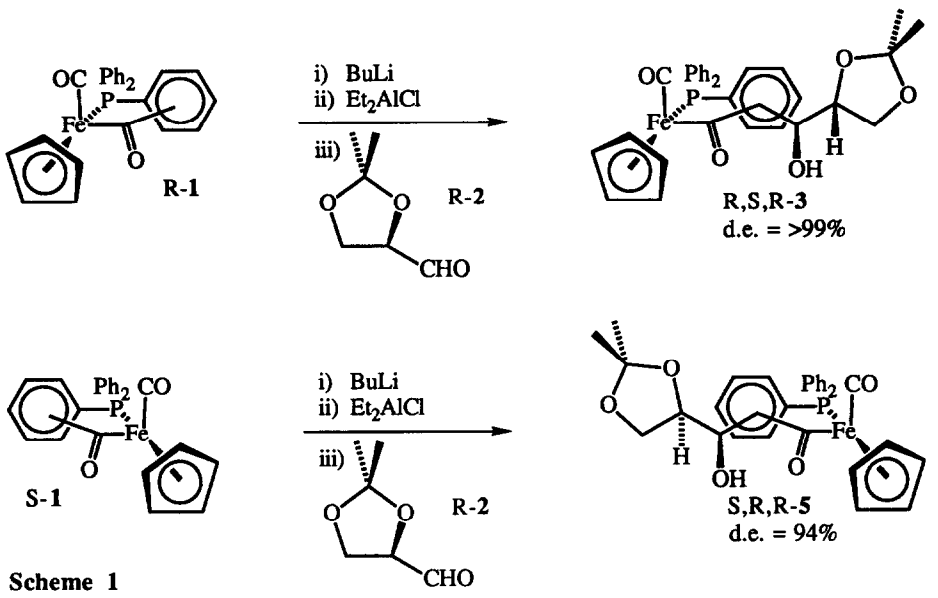
The asymmetric aldol reaction is a method of fundamental importance for the asymmetric synthesis of carbon-carbon bonds[1]. A number of successful approaches to the synthesis of chiral auxiliaries capable of exerting high levels of stereocontrol over the reactions of attached propionate enolates have been reported both by us[2] and others[3] that have allowed asymmetric aldol reactions to be developed. We have previously shown that the diethylaluminium enolate derived from the iron acetyl complex **1** undergoes highly diastereoselective (>99 : 1) aldol reactions with simple achiral aldehydes in good chemical yield[4]. This reagent **1** may thus be deprotonated to give a chiral acetate equivalent, which offers the advantages of high levels of stereoselectivity in reactions with a wide range of electrophiles[5] and which may display complementary reactivity with different enolate counterions[6]. In an extension of this work we have described the use of this chiral acetate equivalent to synthesise pyrrolizidine alkaloids in which the chiral auxiliary successfully overcomes the inherent diastereofacial selectivity associated with the stereogenic centre in the electrophile[7]. In this latter reaction, the two enantiomers of complex **1** reacted with (S)-N-Boc-prolinal with different diastereoselectivities in a manner that was in agreement with the simple model proposed by Masamune for the combination of two chiral reagents to

generate one or more new stereogenic centre(s)[8]. This model of double asymmetric induction states that, so long as the transition states of the two chiral reagents are mutually accommodating, the levels of diastereoselection can be calculated approximately from a knowledge of the diastereoselectivities the two reagents show in reactions with achiral partners. In the 'matched pair reaction', the two reagents interact cooperatively and there is an increase in the overall stereoselectivity of the reaction. The Masamune model proposes that, as each of the stereoselectivities may be related to a difference of free energy between two diastereoisomeric transition states, the overall reaction diastereoselectivity will correspond to the sum of the two individual free energy differences, so long as the two control elements do not perturb one another. This has the effect that in an ideal system, the diastereoselectivity of the matched pair reaction will be the product of the individual reagent diastereoselectivities. Conversely, in the mismatched pair reaction, the overall reaction diastereoselectivity will correspond to the difference between the two free energy terms and it is found that the overall stereoselectivity is equal to the quotient of the two diastereoselectivities. At the time we commenced this work, we were unaware of an example of a reaction which departed significantly from this postulate. As diethylaluminium enolates of iron acyl complexes have been demonstrated to react *via* highly-ordered 'boat-like' transition states in aldol reactions, we wished to investigate whether the Masamune model would be generally valid for the reactions between these enolates and chiral aldehydes.

Heathcock[9] has demonstrated that addition of enolates to 2,3-O-isopropylidene-D-glyceraldehyde **2** may occur under both chelation and non-chelation control. The former favours attack on the *Re* face whereas under non-chelation control the Felkin-Anh model[10,11] predicts that attack will occur preferentially on the *Si* face. As this aldehyde is readily prepared in homochiral form *via* the oxidative cleavage of 1,2;5,6-di-O-isopropylidene-D-mannitol with lead tetra-acetate[12], it seemed an ideal candidate for the study of these reactions. Furthermore, the cleavage of 1,2;5,6-di-O-isopropylidine-D-sorbitol would allow the synthesis of the same aldehyde in racemic form but under the same reaction conditions. The stability of the homochiral R aldehyde with respect to polymerisation and racemisation has been questioned[13]. However, it was found that THF solutions of the aldehyde were stable at -30°C for extended periods although the aldehyde was generally prepared immediately prior to use.

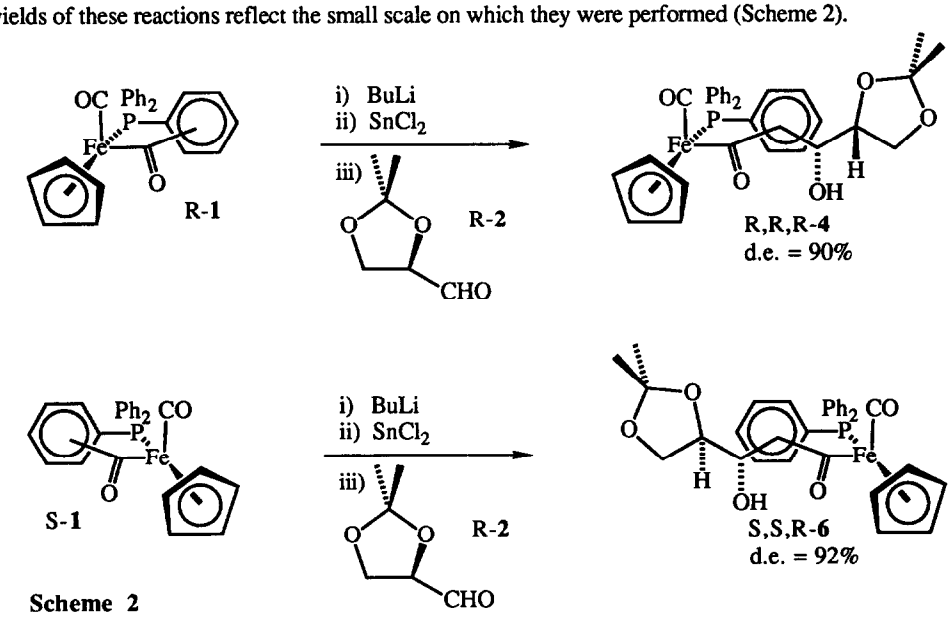
The diethylaluminium enolate derived from homochiral iron acetyl complex (R)-**1** was reacted with an excess of aldehyde (R)-**2** at -100°C over a reaction period of 3 h to give a mixture of starting complex **1** and aldol product **3**. In the ^{1}H n.m.r. spectrum of the crude product of this reaction, only a single diastereoisomer (R,S,R)[14]-**3** of the product was observable (with no sign of the R,R,R diastereoisomer **4**) and, after chromatographic removal of the starting material (30%), this was isolated in a yield of 26%. The reaction was repeated using the S enantiomer of the enolate to give a crude product that contained some starting complex **1** (25%) as well as the two diastereoisomers, **5** and **6**, of the aldol product in a ratio of 97 : 3. The combined yield of these two diastereoisomers, after chromatographic removal of (R)-**1** was 25% (Scheme 1).

In these reactions the R enantiomer of the iron enolate forms the matched pair reaction with the R enantiomer of the aldehyde as this reaction is the more selective. Thus, the R,S,R diastereoisomer **3** is favoured by both the inherent diastereofacial bias of the aldehyde and the much larger stereodirecting effect of the iron chiral auxiliary. In the mismatched pair reaction the S,R,R diastereoisomer **5** is favoured by the iron acyl enolate but opposed by the aldehyde whilst the S,S,R diastereoisomer **6** is favoured by the aldehyde but opposed by the enolate. The observed stereoselectivities are consistent with the iron acyl enolate showing a stereoselectivity of ~99 : 1 and the aldehyde a selectivity of ~70 : 30.



Scheme 1

The tin (II) enolate derived from the R enantiomer of complex **1** was reacted with aldehyde (R)-**2** at -78°C and the reaction allowed to warm to ambient temperature over 15 h. The crude product contained some recovered starting complex and a 5 : 95 mixture of the two possible aldol diastereoisomers **3** and **4** in a yield of 24% after removal of recovered (S)-**1** (58%). Repetition of this reaction with the S enantiomer of complex **1** gave some recovered starting material as well as a 4 : 96 mixture of diastereoisomers **5** and **6** in a yield, after chromatography, of 38%. The two product distributions suggest that the inherent diastereoselectivity of the aldehyde has very little effect in these reactions with the iron enolate showing a diastereoselectivity of 95 : 5. The low yields of these reactions reflect the small scale on which they were performed (Scheme 2).



Scheme 2

Although these four reactions had allowed the stereoselective synthesis of all four diastereoisomers of the β–hydroxy acyl complex, the assignment of configuration had still to be made. Of the three stereogenic centres in each compound (which will be listed in linear order starting from the iron centre, then the β-hydroxy and γ-alkoxy centre stereogenic centres), the first was known on the basis of which enantiomer of the enolate had been employed whilst the third was consistently R as only this enantiomer of the aldehyde, derived from D-mannitol, had been used. The relative stereochemistry between the iron centre and the newly-formed β-hydroxy centre may be established on the basis of the correlation of ^{1}H n.m.r. data to known crystal structures of aldol products[4,6]. In simple systems, containing only these two stereogenic centres, the methylene group α- to the iron acyl carbonyl group of the diastereoisomer formed as the major product in the reaction of a diethylaluminium enolate shows a smaller chemical shift difference between the two diastereotopic protons than is observed in the other diastereoisomer[6]. In general it is found that this manifests itself in the resonances due to these two protons lying between those due to the same two protons in the other diastereoisomer. Table 1 below shows the chemical shifts at which these proton resonances were recorded. Both the diastereoisomers obtained as major products in the reactions of homochiral diethylaluminium enolates showed a smaller difference in the chemical shifts for these two protons. Even though the resonances for **3** did not lie directly within those of **4**, all four diastereoisomers were assigned in this way and this gave the products expected on the basis of the transition states already proposed for these reactions.

Table 1 Chemical shifts (/ppm) for the diastereotopic $COCH_2$ methylene protons of diastereoisomers **3-6**

Configuration at Iron	R	R	S	S
Enolate Counterion	Et_2Al	Sn (II)	Et_2Al	Sn (II)
δ / ppm	3.42	3.11	2.93	3.39
	3.04	2.52	2.70	2.53
Configuration[14]	R,S,R	R,R,R	S,R,R	S,S,R
Compound	**3**	**4**	**5**	**6**

With all four possible β-hydroxy acyl products characterised, reactions using racemic enolates could now be investigated and the product ratios determined from ^{1}H n.m.r. spectra. As racemic **2** could readily be prepared from D-sorbitol, reactions with either both reagents present in racemic form or with the racemic enolate and homochiral aldehyde could be attempted. The results of these reactions using racemic diethylaluminium and tin (II) enolates are presented below (Table 2). In all cases, the major products obtained above in the reactions of homochiral enolates were the predominant products obtained in the reactions of the racemic enolates. Thus, the major products of these reactions may be seen in Schemes 1 and 2. For clarity the reactions of homochiral enolates are also included in the table below (Table 2).

Table 2 Product ratios for reactions of racemic diethylaluminium and tin (II) enolates derived from complex **1**

Enolate	Counterion	Aldehyde	Temperature	3	4	5	6
RS-1	Et_2Al	R-2	-100°C	64	<1	35	1
R-1	Et_2Al	R-2	-100°C	>99	<1	–	–
S-1	Et_2Al	R-2	-100°C	–	–	97	3
RS-1	Et_2Al	RS-2	-100°C	65	2	28	5
RS-1	Sn (II)	R-2	-78°C	3	36	<1	61
R-1	Sn (II)	R-2	-78°C	5	95	–	–
S-1	Sn (II)	R-2	-78°C	–	–	4	96
RS-1	Sn (II)	RS-2	-78°C	5	28	2	65
RS-1	Sn (II)	R-2	-100°C	5	35	3	57
R-1	Sn (II)	R-2	-100°C	0	0	–	–
S-1	Sn (II)	R-2	-100°C	–	–	4	96

In the reaction of the racemic diethylaluminium enolate the observed product ratio suggests that the two chiral reagents are reacting with similar diastereoselectivities to those recorded for the reactions using homochiral enolates. It is clear from the product distribution in the diethylaluminium enolate reaction that the ratio of products derived from the R enantiomer of complex **1** to those derived from the S enantiomer is approximately 65 : 35. This should result in any recovered starting material being enriched in the S enantiomer as this is the enantiomer which forms the mismatched pair with the R enantiomer of **2**. In the second reaction, with the tin (II) enolate, the reversal in the stereoselectivity of the enolate causes the R enantiomer to be the one that forms the mismatched pair reaction with (R)-**2**. For both these reactions the recovered starting material was enriched in the enantiomer that forms the mismatched pair although quantitative agreement with the value calculated from the ratio of products could not be achieved due to incomplete mass balance.

That tin (II) enolates react less stereoselectively than do diethylaluminium enolates has been noted before, as has the observation that the diastereoselectivity in the aldol reactions of diethylaluminium enolates drops off dramatically as the temperature is raised from -100°C to -78°C. As may be seen in the table above, repeating the reaction of the tin (II) enolate derived from racemic **1** with (R)-**2** at -100°C did cause the electrophile to show a greater diastereofacial bias but did not cause a significant increase in the stereoselectivity of the enolate. When the reaction was repeated with homochiral enolates, the S enantiomer, which forms the matched pair in this reaction with (R)-**2** gave a 4 : 96 mixture of diastereoisomers **5** and **6** but the R enantiomer of complex **1** failed to react, giving only recovered starting material. This would seem to be indirect evidence for the existence of these tin (II) enolates in aggregated form. If the racemic enolate consisted of discrete non-aggregated enolates, the homochiral enolates would react in an identical manner to the racemate. That there is a discrepancy in these reactions suggests, that for the racemate at least, aggregation of the enolate is occurring. The aggregation of metal enolates has been widely reported[15] although this is the first example in which iron acyl enolates have shown this effect.

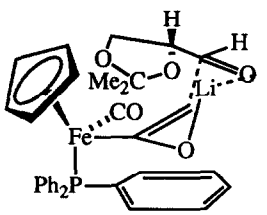
Apart from the effect of enolate aggregation, all the reactions described above could be made to agree qualitatively with the Masamune model although the stereoselectivity of the aldehyde, as calculated from the product ratio did vary. However, the diastereofacial bias that it showed was always in favour of attack on the *Si* face, consistent with the Felkin-Anh model[10,11] and suggesting that the reaction was proceeding under non-chelation control. Lithium enolates have been shown to add to aldehyde **2** under chelation control[9] although the diastereoselectivities shown by lithium enolates derived from complex **1** in aldol reactions are low[12]. Addition of the racemic lithium enolate of **1** was found to occur to the *Si* face of aldehyde **2** when addition was performed at -78°C. The product ratio (Table 3) also indicated that the iron acyl enolate showed a diastereoselectivity in the same sense, although of a much lower magnitude, as was observed for the diethylaluminium enolates.

The reaction was repeated at -100°C which did give addition predominantly to the *Re* face of (R)-2, suggesting that chelation controlled addition was occurring. Furthermore this reversal in the diastereoselectivity of the aldehyde had caused a concomitant reversal in the diastereoselectivity of the enolate, so that it parallelled the reactivity of the tin (II) enolate.

Table 3 Product ratios and yields for reactions of racemic lithium enolates of complex **1** with aldehyde **(R)-2**

Enolate	Counterion	Aldehyde	Temperature	3	4	5	6
RS-1	Li	R-2	-78°C	50	8	17	25
RS-1	Li	R-2	-100°C	8	50	25	17

This reversal of diastereoselectivity, although only relating to quite small selectivities, has not been observed before. Although it is possible that the low diastereoselectivity of the lithium enolate reaction is a consequence of an open transition state, it could also be the result of a closed transition state which is not sufficiently tightly held to allow full chirality transfer. At lower temperature, where intramolecular chelation becomes more favourable, transition state **8** becomes of lowest energy. To allow the α-alkoxy group to chelate to the lithium, this substituent must be in an axial or pseudo-axial position. In the chair-like transition state **7**, this substituent adopting an axial position would project it into the cyclopentadienyl ligand and thus, transition state **8** is adopted causing a reversal in the stereodirecting nature of the enolate from that which it showed before (Scheme 3).



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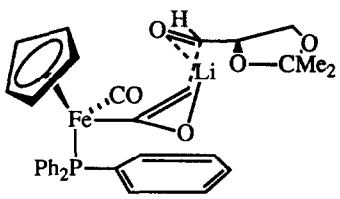

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Scheme 3

Thus, this represents a deviation from the result expected on the basis of the Masamune model. The transition state through which the lithium enolate of **1** reacts cannot allow the aldehyde to chelate the α-alkoxy

group to the enolate counterion: the two transition states are not mutually accommodating. A caveat to this argument must be that the reversal of selectivity can only occur because the normal diastereoselectivity shown by the lithium enolate is very small and the energy loss in perturbing its idealised transition state is commensurately small.

Conclusion: All four diastereoisomers of the β-hydroxy acyl complex resulting from addition of an enolate derived from iron acetyl complex **1** to aldehyde (R)-**2** may readily be prepared, in high diastereoisomeric excess, merely by varying the enantiomer of the chiral auxiliary and the counterion of the enolate. In all cases the high levels of diastereoselection exhibited by the enolate of the iron acyl complex completely overcome the inherent diastereofacial bias of the aldehyde. To date, no other chiral auxiliary can provide this facility.

Experimental: *General* - All manipulations of organometallic complexes were performed under an atmosphere of nitrogen with deoxygenated solvents and using standard vacuum line and Schlenk tube techniques[16]. *n*-Butyllithium was used as a 1.6M solution in hexanes and diethylaluminiumchloride as a 2.0M solution in toluene. Tin (II) chloride was dried by stirring with acetic anhydride for 48 h, washing with sodium-dried ether and drying vacuo for 120 h. Tetrahydrofuran was dried over sodium benzophenone ketyl and distilled.

Melting points were determined using a Gallenkamp apparatus and are uncorrected. Optical rotations at the sodium D line were recorded on a Perkin-Elmer 241 polarimeter at 23°C. Elemental analyses were performed by the Dyson Perrins analytical department. Infra-red spectra were recorded in dichloromethane solution on Perkin-Elmer 297 and 781 spectrophotometers. ^{1}H n.m.r. spectra were recorded on a Bruker WH300 (300.13 MHz) spectrometer whereas ^{13}C and ^{31}P n.m.r. spectra were recorded on a Bruker AM250 (^{13}C; 62.90 MHz. ^{31}P; 101.26 MHz) instrument. Spectra were recorded in $CDCl_3$ solution at ambient temperature. Mass spectra were obtained on a V.G. Micromass ZAB 1F instrument using field-desorption techniques.

(R,S,R)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH$_2$CH(OH)C$_5$H$_9$O$_2$] **3** - Generation of the diethylaluminium enolate from the R enantiomer of iron acetyl complex (R)-**1** (200 mg, 0.44 mmol) followed by addition of 2,3-0-isopropylidene-D-glyceraldehyde (R)-**2** (626 mg, 4.80 mmol as a solution in THF at -78°C) with stirring (-100°C, 3 h) gave, after work-up and chromatography, starting complex (R)-**1** (37 mg) and a 99 : <1 mixture of the (R,S,R)-**3** and (R,R,R)-**4** diastereoisomers (40 mg, 26%). (Found; C, 65.75; H, 5.99; P, 5.15. $C_{32}H_{33}FeO_5P$ requires C, 65.77; H, 5.69; P, 5.30%). Major diastereoisomer **3**, υ_{max} ($CHCl_3$)/cm^{-1} 3400 (OH), 1921 (C≡O) and 1590 (C=O); δ_H (300 MHz, $CDCl_3$) 7.51-7.35 (15H, m, PPh_3), 4.44 (5H, d, J_{PH} 1.2 Hz, Cp), 3.94, 3.67 (2H, ABX system, J_{AB} 7.8 Hz, $CH_2OC(CH_3)_2$), 3.76 (1H, m, CH(OH)), 3.24 (1H, m,, $CHOC(CH_3)_2$), 3.04 (1H, br s, CH(OH)), 3.42, 3.04 (2H, ABX system, J_{AX} 3.6 Hz, J_{BX} 5.8 Hz, $COCH_2$), 1.38 (3H, s, CH_3) and 1.32 (3H, s, CH_3); δ_C (62.9 MHz, $CDCl_3$) 220.2 (d, J_{PC} 30.6 Hz, Fe-(CO)), 136.1 (d, J_{PC} 43.7 Hz, PPh_3C_{ipso}), 133.3 (d, J_{PC} 10.2 Hz, PPh_3C_{ortho}), 129.9 (s, PPh_3C_{para}), 128.2 (d, J_{PC} 9.6 Hz, PPh_3C_{meta}), 109.2 (d, $C(CH_3)_2$), 85.5 (s, Cp), 77.9 (s, CH(OH)), 69.2 (s, $CHOC(CH_3)_2$), 67.5 (s, $COCH_2$), 65.5 (s, $CH_2OC(CH_3)_2$), 26.5 (s, CH_3) and 25.5 (s, CH_3); δ_P (101.3 MHz, $CDCl_3$) 71.48 (s); *m/z* 584(M^+), 556(M^+-28).

(R,R,R)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH$_2$CH(OH)C$_5$H$_9$O$_2$] **4** - Generation of the tin (II) enolate from the R enantiomer of iron acetyl complex (R)-**1** (130 mg, 0.29 mmol) followed by addition of 2,3-0-isopropylidene-D-glyceraldehyde (R)-**2** (282 mg, 2.20 mmol as a solution in THF at -78°C) with stirring (15 h,

warming from -78°C to room temperature) gave, after work-up and chromatography, starting complex (R)-**1** (58 mg) and a 5 : 95 mixture of the (R,S,R)-**3** and (R,R,R)-**4** diastereoisomers (22 mg, 24%). Major diastereoisomer **4**, υ_{max} ($CHCl_3$)/cm^{-1} 3400 (OH) and 1922 (C≡O); δ_H (300 MHz,,$CDCl_3$) 7.59 - 7.39 (15H, m, PPh_3), 4.45 (5H, d, J_{PH} 1.2 Hz, Cp), 3.86, 3.56 (2H, ABX system, J_{AB} 7.6 Hz, J_{AX} 5.0 Hz, J_{BX} 6.2 Hz, $CH_2OC(CH_3)_2$), 3.78 (1H, m, CH(OH)), 2.72 (1H, d, J 3.9 Hz, CH(OH)), 3.91 (1H, m, $CHOC(CH_3)_2$), 3.11, 2.52 (2H, ABX system, J_{AB} 16.6 Hz, J_{AX} 3.0 Hz, J_{BX} 9.0 Hz, $COCH_2$), 1.42 (3H, s, CH_3) and 1.33 (3H, s, CH_3); δ_C (62.9 MHz, $CDCl_3$) 219.9 (d, J_{PC} 25.6 Hz, Fe-(CO)), 136.1 (d, J_{PC} 43.3 Hz, PPh_3C_{ipso}), 133.2 (d, J_{PC} 9.8 Hz, PPh_3C_{ortho}), 129.8 (s, PPh_3C_{para}), 128.1 (d, J_{PC} 9.7 Hz, PPh_3C_{meta}), 109.1 (s, $C(CH_3)_2$), 85.2 (s, Cp), 77.5 (s, CH(OH)), 69.9 (s, $CHOC(CH_3)_2$), 66.9 (s, $COCH_2$), 65.5 (s, $CH_2OC(CH_3)_2$), 26.7 (s, CH_3) and 25.3 (s, CH_3); ^{31}P n.m.r. δ_P (101.3 MHz, $CDCl_3$) 72.47 (s); *m/z* 584 (M^+), 556 (M^+-28). In a similar fashion, reaction of the homochiral tin (II) enolate derived from (R)-**1** with homochiral aldehyde (R)-**2** at temperatures below -78°C was undertaken by adding a solution of 2,3-0-isopropylidene-D-glyceraldehyde (R)-**2** (604 mg, 4.60 mmol) in THF at room temperature to a solution of the tin (II) enolate (derived from 200 mg, 0.44 mmol of acetyl complex (R)-**1**) in THF at -100°C. After a standard reaction period, work-up gave only recovered starting complex (S)-**1** (178 mg).

(S,R,R)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OH)C_5H_9O_2$] **5** - Under identical reaction conditions to those used above with the R enantiomer, reaction of the S enantiomer of complex (S)-**1** with (R)-**2** gave 49 mg of recovered starting complex (S)-**1** and a 97 : 3 mixture of the (S,R,R)-**5** and (S,S,R)-**6** diastereoisomers (38 mg, 25%). (Found; C, 65.90; H, 5.84; P, 5.60. $C_{32}H_{33}FeO_5P$ requires C, 65.77; H, 5.69; P, 5.30%). Major diastereoisomer **5**, υ_{max} ($CHCl_3$)/cm^{-1} 3400 (OH), 1921 (C≡O) and 1590 (C=O); δ_H (300 MHz, $CDCl_3$) 7.65-7.37 (15H, m, PPh_3), 4.46 (5H, d, J_{PH} 1.2 Hz, Cp), 3.78, 3.41 (2H, ABX system, J_{AB} 14.1 Hz, J_{AX} 7.3 Hz, J_{BX} 6.2 Hz, $CH_2OC(CH_3)_2$), 3.71 (1H, m, CH(OH)), 3.35 (1H, d, J 2.7 Hz, CH(OH)), 3.25 (1H, m, $CHOC(CH_3)_2$), 2.93, 2.70 (2H, ABX system, J_{AB} 17.3 Hz, J_{AX} 2.3 Hz, J_{BX} 9.6 Hz, $COCH_2$), 1.39 (3H, s, CH_3) and 1.32 (3H, s, CH_3); δ_C (62.9 MHz, $CDCl_3$) 220.2 (d, J_{PC} 30.6 Hz, Fe-(CO)), 136.1 (d, J_{PC} 43.7 Hz, PPh_3C_{ipso}), 133.3 (d, J_{PC} 10.2 Hz, PPh_3C_{ortho}), 129.9 (s, PPh_3C_{para}), 128.2 (d, J_{PC} 9.6 Hz, PPh_3C_{meta}), 109.0 (s, $C(CH_3)_2$), 85.4 (s, Cp), 77.9 (s, CH(OH)), 70.2 (s, $CHOC(CH_3)_2$), 67.4 (s, $COCH_2$), 66.9 (s, $CH_2OC(CH_3)_2$), 26.7 (s, CH_3) and 25.4 (s, CH_3); ^{31}P n.m.r. δ_P (101.3 MHz, $CDCl_3$) 72.19 (s); *m/z* 584 (M^+), 556 (M^+-28).

(S,S,R)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OH)C_5H_9O_2$] **6** - Generation of the tin (II) enolate from the S enantiomer of iron acetyl complex (S)-**1** (188 mg, 0.42 mmol) followed by addition of 2,3-0-isopropylidene-D-glyceraldehyde (R)-**2** (282 mg, 2.20 mmol as a solution in THF at -78°C) with stirring (15 h, warming from -78°C to room temperature) gave, after work-up and chromatography, starting complex (R)-**1** (104 mg) and a 5 : 95 mixture of the (S,R,R)-**5** and (S,S,R)-**6** diastereoisomers (41 mg, 38%). Major diastereoisomer **6**, υ_{max} ($CHCl_3$)/cm^{-1} 3400 (OH), 1922 (C≡O) and 1589 (C=O); δ_H (300 MHz, $CDCl_3$) 7.57-7.38 (15H, m, PPh_3), 4.44 (5H, d, J_{PH} 1.2 Hz, Cp), 3.94, 3.79 (2H, ABX system, J_{AB} 8.4 Hz, J_{AX} 5.0 Hz, J_{BX} 6.0 Hz, $CH_2OC(CH_3)_2$), 3.65 (1H, m, CH(OH)), 3.65 (1H, m, $CHOC(CH_3)_2$), 3.39, 2.53 (2H, ABX system, J_{AB} 17.6 Hz, J_{AX} 1.6 Hz, J_{BX} 9.0 Hz, $COCH_2$), 2.81 (1H, d, J 2.1 Hz, CH(OH)), 1.39 (3H, s, CH_3) and 1.33 (3H, s, CH_3); δ_C (62.9 MHz, $CDCl_3$) 220.0 (d, J_{PC} 25.6 Hz, Fe-(CO)), 136.0 (d, J_{PC} 43.4 Hz, PPh_3C_{ipso}), 133.2 9d, J_{PC} 9.8 Hz, PPh_3C_{ortho}), 129.8 (s, PPh_3C_{para}), 128.1 (d, J_{PC} 9.7 Hz,

PPh_3C_{meta}), 108.9 (s, $C(CH_3)_2$), 85.1 (s, Cp), 77.5 (s, CH(OH)), 68.7 (s, $CHOC(CH_3)_2$), 66.9 (s, $COCH_2$), 65.5 (s, $CH_2OC(CH_3)_2$), 26.4 (s, CH_3) and 25.4 (s, CH_3); δ_P (101.3 MHz, $CDCl_3$) 71.79 (s); *m/z* 584 (M^+), 556 (M^+-28). In a similar fashion, reaction of the homochiral tin (II) enolate derived from (S)-**1** with homochiral aldehyde (R)-**2** at temperatures below -78°C was undertaken by adding a solution of 2,3-0-isopropylidene-D-glyceraldehyde (R)-**2** (604 mg, 4.60 mmol) in THF at room temperature to a solution of the tin (II) enolate (derived from 200 mg, 0.44 mmol of acetyl complex (S)-**1**) in THF at -100°C. This gave a 1 : 99 mixture of the (S,R,R)-**5** and (S,S,R)-**6** diastereoisomers (22 mg, 31%) together with some starting complex (S)-**1** (145 mg).

Reaction of the diethylaluminium enolate derived from (RS)-**1** *with* (R)-**2** - Generation of the diethylaluminium enolate from racemic iron acetyl complex (RS)-**1** (500 mg, 1.10 mmol) followed by addition of 2,3-di-O-isopropylidene-D-glyceraldehyde (R)-**2** (564 mg, 4.37 mmol as a solution in THF at -78°C) with stirring (-100°C, 3 h) gave, after work-up and chromatography some starting complex **1** (388 mg) and the mixture of the four diastereoisomers **3-6** shown in Table 2 (126 mg, 87%).

Reaction of the tin (II) enolate derived from (RS)-**1** *with* (R)-**2** - Addition of a solution of aldehyde (R)-**2** (1.00 g, 7.70 mmol) in THF at -78°C to a solution of the tin (II) enolate (derived from 2.00 g, 4.40 mmol of complex (RS)-**1** in THF at -78°C with stirring (15 h, warming from -78°C to room temperature) led to the formation of the mixture of diastereoisomers **3-6** shown in Table 2 (643 mg, 95%) and some starting complex **1** (1.48 g). In the analogous reaction, with addition of a solution of 2,3-di-O-isopropylidene-D-glyceraldehyde (R)-**2** (656 mg, 5.05 mmol) in THF at room temperature to a solution of the racemic tin (II) enolate (derived from 500 mg, 1.10 mmol of complex (RS)-**1** in THF at -100°C, the mixture of diastereoisomers **3-6** shown in Table 2 (112 mg, 74%) was formed with some starting complex **1** (381 mg).

Reactions of the diethylaluminium enolate derived from (RS)-**1** *with* (RS)-**2** - Reaction of the diethyl aluminium enolate derived from 500 mg (1.10 mmol) of complex (RS)-**1** with 472 mg (3.63 mmol) of racemic aldehyde (RS)-**2** under the conditions described previously gave 117 mg (40%) of the mixture of diastereoisomers **3-6** shown in Table 2 and 274 mg of starting complex (RS)-**1**.

Reactions of the tin (II) enolate derived from (RS)-**1** *with* (RS)-**2** - Addition of a solution of racemic aldehyde (RS)-**2** (472 mg, 3.63 mmol) in THF at -78°C to a solution of the tin (II) enolate (derived from 500 mg, 1.10 mmol of complex (RS)-**1** also at -78°C with stirring (15 h, warming from -78°C to room temperature) gave 40 mg (31%) of the mixtrue of diastereoisomers **3-6** shown in Table 2 and 400 mg of starting complex (RS)-**1**.

Reactions of the lithium enolate derived from (RS)-**1** *with* (R)-**2** - Analogous reactions to those described above for tin (II) enolates were undertaken with the lithium enolate. The reaction with addition occurring at -78°C used an enolate derived from complex (RS)-**1** (500 mg, 1.10 mmol) and of aldehyde (R)-**2** (612 mg, 4.65 mmol) and gave 164 mg (80%) of the mixture of diastereoisomers **3-6** shown in Table 3 and 340 mg of starting complex (RS)-**1**. The reaction with addition occurring above -78°C used an enolate derived from

complex (RS)-**1** (1.00 g, 2.20 mmol) and aldehyde (R)-**2** (572 mg, 4.41 mmol) and gave 610 mg (72%) of the mixture of diastereoisomers shown in Table 3 and 337 mg of starting complex (RS)-**1**.

Reactions of the lithium enolates derived from (R)-**1** *and* (S)-**1** *with* (R)-**2**.- The reactions were performed as described above for (RS)-**1** at -78°C and allowed to warm slowly to 20°C before work-up. In both cases the separation of diastereoisomers was readily achieved by chromatography (SiO_2; ether : petrol, 1 : 1) to give after recrystallisation from ether-hexane pure samples of each diastereoisomer. The reaction of (R)-**1** gave (R,S,R)-**3** (46%), (R,R,R)-**4** (33%) and 18% recovered (R)-**1** (mass balance 97%). The reaction of (S)-**1** gave (S,R,R)-**5** (37%), (S,S,R)-**6** (53%) and 8% recovered (S)-**1** (mass balance 98%).
(R,S,R)-**3**: m.p. 61-4°C; $[\alpha]_D^{23}$ -89.9 (c = 1.0, $CHCl_3$); Found; C, 65.83; H, 5.99. $C_{32}H_{33}FeO_5P$ requires C, 65.77; H, 5.69. (R,R,R)-**4**: m.p. 42-4°C; $[\alpha]_D^{23}$ -65.3 (c = 1.0, $CHCl_3$); Found; C, 65.78; H, 5.85. $C_{32}H_{33}FeO_5P$ requires C, 65.77; H, 5.69. (S,R,R)-**5**: m.p. 53-6°C; $[\alpha]_D^{23}$ +105.9 (c = 1.0, $CHCl_3$); Found; C, 65.73; H, 5.53. $C_{32}H_{33}FeO_5P$ requires C, 65.77; H, 5.69. (S,S,R)-**6**: m.p. 56-8°C; $[\alpha]_D^{23}$ +58.1 (c = 1.0, $CHCl_3$); Found; C, 65.66; H, 5.72. $C_{32}H_{33}FeO_5P$ requires C, 65.77; H, 5.69.

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References

1. C.H. Heathcock in *Asymmetric Synthesis*, ed. J.D. Morrison, Academic Press, New York, 1984, vol. 3, ch.2; D.A. Evans, J.V. Nelson and T.R. Taber, *Top. Stereochem.*, 1982, **13**, 1.
2. S.G. Davies, *Aldrichimica Acta.*, 1990, **23**, 31; S.G. Davies and A.A. Mortlock, *Tetrahedron Lett.*, 1991, **32**, 4787.
3. D.A. Evans, J. Bartroli and T.L. Shih, *J. Am. Chem. Soc.*, 1981, **103**, 2127; D.A. Evans, *Aldrichimica Acta.*, 1982, **15**, 23; W. Oppolzer, *Tetrahedron*, 1987, **43**, 1969.
4. S.G. Davies, I. Dordor-Hedgecock, P. Warner, R.H. Jones and K. Prout, *J. Organomet. Chem.*, 1985, **285**, 213.
5. S.G. Davies, R. Polywka and P. Warner, *Tetrahedron*, 1990, **46**, 4847.
6. L.S. Liebeskind, M.E. Welker and R.W. Fengl, *J. Am. Chem. Soc.*, 1986, **108**, 6328.
7. R.P. Beckett and S.G. Davies, *J. Chem. Soc., Chem. Commun.*, 1988, 160.
8. S. Masamune, W. Choy, J.S. Petersen and L.R. Sita, *Angew. Chem. Int. Ed. Engl.*, 1985, **24**, 1.
9. C.H. Heathcock, S.D. Young, J.P. Hagen, M.C. Pirrung, C.T. White and D. VanDerveer, *J. Org. Chem.*, 1980, **45**, 3846.
10. M. Cherest, H. Felkin and N. Prudent, *Tetrahedron Lett.*, 1968, **9**, 2199.
11. N.T. Anh and O. Eisenstein, *Nouv. J. Chem.*, 1977, **1**, 61.
12. R. Dumont and H. Pfander, *Helv. Chim. Acta.*, 1983, **66**, 814.
13. C.R. Schmid, J.D. Bryant, M. Dowlatzedah, J.L. Phillips, D.E. Prather, R.E. Schantz, N.L. Sear and C.S. Vianco, *J. Org. Chem.*, 1991, **56**, 4056.
14. For all complexes the configuration at iron is listed first followed by those in the acyl ligand.
15. D. Seebach, *Angew. Chem. Int. Ed. Engl.*, 1988, **27**, 1624.
16. D.F. Shriver, *The Manipulation of Air-Sensitive Compounds*, McGraw Hill, New York, 1969.