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CHIRAL ACETATE ENOLATE EQUIVALENT FOR THE SYNTHESIS OF β-HYDROXY ACIDS AND ESTERS: X-RAY CRYSTAL STRUCTURE OF *RR,SS*-[(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_2CH_3$)]

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Summary

The aluminium enolate derived from the iron acetyl complex [(η^5-C_5H_5)Fe(CO)-(PPh_3)$COCH_3$], in contrast to the lithium enolate, undergoes highly stereoselective aldol reactions with aldehydes to generate *RR,SS*-β-hydroxyacyl complexes which on decomplexation liberate β-hydroxy acids or esters. Determination of the molecular structure of *RR,SS*-[(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_2CH_3$] allowed assignment of the relative configuration of the new chiral centre.

One of the most fundamental in vitro and in vivo carbon–carbon bond forming reactions is the aldol condensation between an enolate and an aldehyde. In synthesis the use of chiral enolates to achieve extremely high stereoselectivities is now well established [1]. However, an essential feature of all of the methods reported to date is the presence of an α-substituent on the enolate. Chiral enolates lacking an α-substituent exhibit little or no stereoselectivity on reaction with aldehydes although some success has been achieved using divalent tin enolates [2]. To date no simple chiral enolate equivalents of acetate or methyl ketones for the aldol reaction have been reported. This problem has however been recently circumvented by the introduction of an α-sulphur substituent (e.g. SMe [3], *p*-tolylSO [4]) which must be removed subsequently by reduction. We have recently reported that lithium enolates derived from the iron acyl complexes (η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2R$ undergo very stereoselective alkylation reactions on treatment with alkyl halides [5]. Furthermore both Liebeskind et al. [6] and ourselves [7] have demonstrated that enolates derived from the acetyl complex (η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_3$) (**1**) react stereoselectively with imines to yield β-amino acyl complexes which on oxidation can be converted to β-lactams. In addition enolates derived from cobaltacyclopentanones

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have been shown to undergo aldol reactions with aldehydes with moderate to good stereoselectivities being observed [8]. We describe here the use of enolates derived from the iron acetyl complex **1** as chiral acetate equivalents for the synthesis of β-hydroxy acids and esters. Part of this work has been the subject of a preliminary communication [9].

Results

Treatment of the readily available acetyl complex **1** * with n-butyllithium in tetrahydrofuran at −78°C for 45 min generates the lithium enolate **2** [5]. Addition of propanal to this solution at −78°C generated after work-up the diastereomeric β-hydroxyl-acyl complexes **4b** and **5b** in the ratio 1.2/1. Addition of anhydrous magnesium bromide to tetrahydrofuran solutions of **2** at −78°C followed by warming to −40°C for 45 min and subsequent addition of propanal at −100°C showed improved stereoselectivity with **4b** and **5b** being formed in the ratio 1.8/1. Similar addition of triisopropoxytitanium chloride gave **4b** and **5b** in the ratio 7/1 whereas a reversed selectivity (**4b**/**5b**, 1/1.2) was observed on addition as above of cuprous cyanide.

Addition of an excess (greater than two-fold) of diethylaluminium chloride, as a solution in toluene, to the lithium enolate **2** at −78°C in tetrahydrofuran followed by warming to −40°C for 45 min to allow transmetallation to occur gave the diethylaluminium enolate **3**. Cooling this solution of **3** to −100°C and subsequent addition of propanal stereoselectively gave **4b** with little of diastereomer **5b** being observed by ^{1}H NMR spectroscopy; the ratio of **4b** to **5b** was assigned as > 100/1, the ^{13}C satellites for **4b** acting as an internal standard corresponding to 0.5%. The yields of **4b** obtained after purification were consistently in the range 86–90%. The relative configurations of the two chiral centres in **4b** were established as *RR*,*SS* by X-ray crystallographic analysis (see below) and confirmed our previous assignments [10].

The results obtained from addition of a range of aldehydes to the lithium enolate **2** and the diethylaluminium enolate **3** are given in Table 1. Little separation of the diastereoisomers was observed on chromatography and/or fractional crystallisation although it was possible to separate diastereoisomers **4f** and **5f** by careful chromatography followed by repeated crystallisations [10]. Satisfactory elemental analyses were obtained for the new β-hydroxy-acyl complexes **4a**–**4e**. Complexes **4f** and **5f** have been previously described [10].

Essentially quantitative decomplexation of the β-hydroxy-acyl complexes **4** prepared from the aluminium enolate **3** can be achieved on addition of bromine to their tetrahydrofuran solutions in the presence of water at 20°C to generate the β-hydroxy acids **6**. Purified yields of these acids were somewhat lower due to known problems in isolation caused by their water solubility. Decomplexation in the presence of anhydrous methanol generated the more readily isolable β-hydroxy esters **7**. The iron bromo complex (η^5-C_5H_5)Fe(CO)(PPh_3)Br could also be isolated from these oxidations in yields of 70–80% after purification.

* All complexes in this paper are racemic. The order of priority for assignment of configuration at iron is C_5H_5 > PPh_3 > CO > COR. For clarity only those with the *R* configuration at iron are shown.

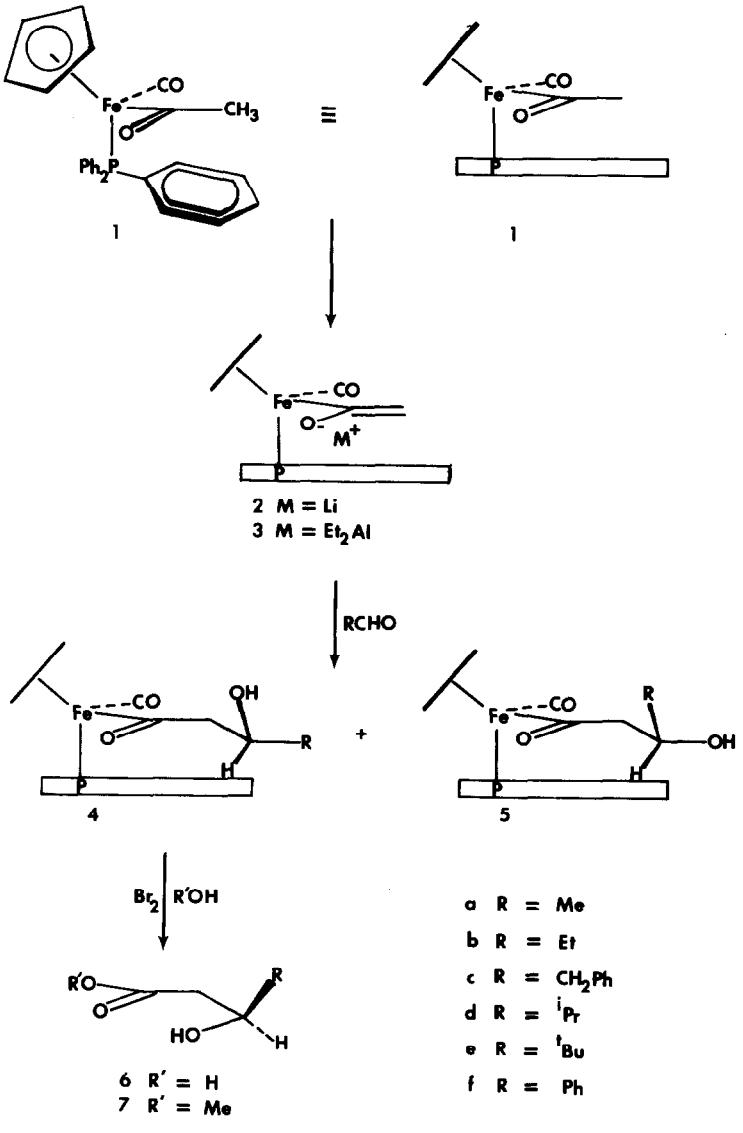


TABLE 1

STEREOSELECTIVITIES (RATIO 4/5) OBTAINED IN THE REACTIONS OF THE LITHIUM 2 AND ALUMINIUM 3 ENOLATES WITH ALDEHYDES (RCHO)

	RCHO	Li-enolate (2)	Et_2Al-enolate (3)
a	MeCHO	1.4/1	24/1
b	EtCHO	1.2/1	>100/1
c	$PhCH_2CHO$	1.5/1	> 20/1
d	i-PrCHO	1.2/1	>100/1
e	t-BuCHO	1.7/1	>100/1
f	PhCHO	1.3/1	20/1

X-ray structure analysis of *RR,SS*-[(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2$-$CH(OH)CH_2CH_3$)] (4b)

Figure 1 shows the X-ray crystal structure of **4b**. Cell parameters and reflection intensities were measured with graphite-monochromated Mo-K_α radiation on an Enraf–Nonius CAD-4 diffractometer operating in the $\omega/2\theta$ scan mode for a crystal having approximate dimensions $0.58 \times 0.58 \times 0.23$ mm. The scan range (ω) was calculated from $[1.00 + 0.35\tan\theta]°$, and the scan speed varied from 1.0 to 6.7° min^{-1} depending upon the intensity. 7633 Reflections were scanned in the range $0 < \theta <$ 27.5. Three standard reflections measured every hour showed no appreciable variation with time. The data were corrected for Lorentz, polarization and absorption effects [11] (relative transmission factors 1.00–1.13) and equivalent reflections were merged to give 6163 unique reflections (R_m 0.008) of which 5028 were considered to be observed [$I > 3\sigma(I)$] and used in the structure analysis.

Crystal data. $C_{29}H_{29}O_3FeP$, $M = 512.4$, triclinic, a 9.259(2), b 10.482(1), c 14.720(3) Å, α 107.04(1), β 105.04(2), γ 92.54(1)°, U 1307.9 $Å^3$, $Z = 2$, D_c 1.30 g cm^{-3}, μ (Mo-K_α 0.71069 Å) = 6.82 cm^{-1}, space group $P1$ or $P\bar{1}$; $P\bar{1}$ established by the analysis.

The structure was solved by Patterson and electron density methods. Following refinement first with isotropic temperature factors and then anisotropically, it was found that the terminal methyl group was disordered. Two orientations of this group were refined with the bond lengths and angles restrained to be close to their expected values [12]. Site occupation factors (constrained to add up to 1) were refined for these two orientations and converged to values of 0.76(1) and 0.24(1). All hydrogen atoms (except those in the disordered portion of the molecule) were found in difference Fourier maps and included in the refinement with restraints being applied to the C–H and the O–H bonds. One common overall temperature factor

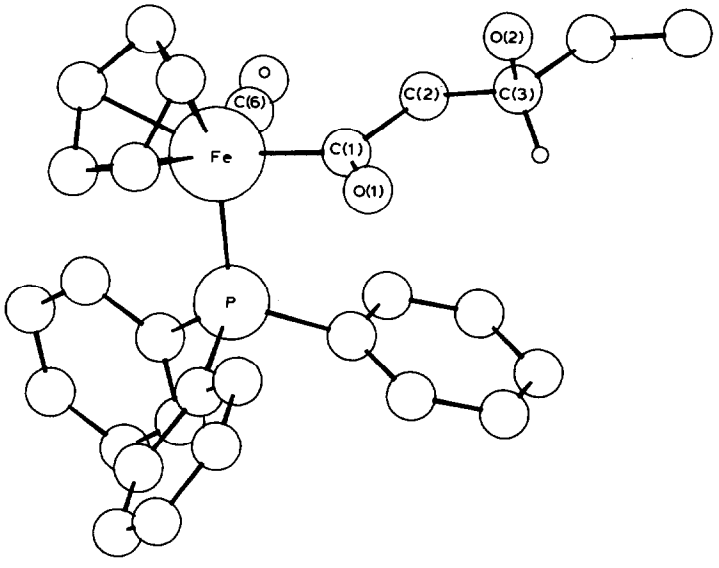


Fig. 1. Molecular structure of *RR,SS*-[(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_2CH_3$)] (**4b**).

TABLE 2

FRACTIONAL ATOMIC COORDINATES AND ISOTROPIC OR EQUIVALENT ISOTROPIC TEMPERATURE FACTORS WITH E.S.D.'S IN PARENTHESES

Atom	x/a	y/b	z/c	U(equiv.) or U(iso)
Fe(1)	−0.47647(2)	0.17393(2)	0.28739(2)	0.0331
P(1)	−0.27708(4)	0.10196(4)	0.24399(3)	0.0303
C(1)	−0.3947(2)	0.1602(2)	0.4208(1)	0.0374
C(2)	−0.3388(3)	0.2883(2)	0.5096(1)	0.0485
C(3)	−0.2965(3)	0.2675(2)	0.6099(1)	0.0549
C(4)	−0.2303(4)	0.4016(3)	0.6912(2)	0.0783
C(5A)	−0.1771(7)	0.3901(5)	0.7938(2)	0.0982
C(5B)	−0.0581(7)	0.423(2)	0.711(1)	0.1203
C(6)	−0.4032(2)	0.3413(2)	0.3187(1)	0.0426
C(7)	−0.6302(2)	0.0636(2)	0.1489(1)	0.0515
C(8)	−0.6380(2)	−0.0004(2)	0.2210(2)	0.0510
C(9)	−0.6836(2)	0.0908(3)	0.2954(2)	0.0555
C(10)	−0.7016(2)	0.2111(3)	0.2727(2)	0.0589
C(11)	−0.6698(2)	0.1931(3)	0.1803(2)	0.0561
C(12)	−0.0985(2)	0.1543(2)	0.3430(1)	0.0343
C(13)	−0.0214(2)	0.0663(2)	0.3857(1)	0.0426
C(14)	0.1094(2)	0.1143(2)	0.4651(1)	0.0501
C(15)	0.1639(2)	0.2486(2)	0.5018(1)	0.0519
C(16)	0.0882(2)	0.3376(2)	0.4588(2)	0.0518
C(17)	−0.0411(2)	0.2910(2)	0.3804(1)	0.0456
C(18)	−0.2282(2)	0.1626(2)	0.1490(1)	0.0358
C(19)	−0.0878(2)	0.1493(2)	0.1321(1)	0.0484
C(20)	−0.0525(2)	0.1927(3)	0.0593(2)	0.0574
C(21)	−0.1556(3)	0.2504(2)	0.0031(1)	0.0546
C(22)	−0.2945(3)	0.2649(2)	0.0190(1)	0.0510
C(23)	−0.3315(2)	0.2214(2)	0.0921(1)	0.0429
C(24)	−0.2857(2)	−0.0816(2)	0.1940(1)	0.0368
C(25)	−0.2526(3)	−0.1465(2)	0.1062(1)	0.0504
C(26)	−0.3314(2)	−0.1588(2)	0.2465(1)	0.0472
C(27)	−0.3403(3)	−0.2980(2)	0.2131(2)	0.0578
C(28)	−0.3055(3)	−0.3608(2)	0.1268(2)	0.0650
C(29)	−0.2619(4)	−0.2855(2)	0.0734(2)	0.0651
O(1)	−0.3943(2)	0.0532(1)	0.43862(9)	0.0481
O(2)	−0.4250(2)	0.2176(2)	0.6310(1)	0.0662
O(3)	−0.3636(2)	0.4534(1)	0.3340(1)	0.0618
H(1)	−0.249(2)	0.333(2)	0.501(2)	0.042(1)
H(2)	−0.418(2)	0.348(2)	0.506(2)	0.042(1)
H(3)	−0.216(2)	0.207(2)	0.610(2)	0.042(1)
H(4A)	−0.311	0.462	0.691	0.1182
H(5A)	−0.144	0.443	0.676	0.1182
H(4B)	−0.254	0.401	0.754	0.1182
H(5B)	−0.277	0.476	0.669	0.1182
H(6A)	−0.136	0.481	0.844	0.1191
H(7A)	−0.262	0.349	0.811	0.1191
H(8A)	−0.096	0.331	0.795	0.1191
H(6B)	−0.016	0.511	0.764	0.1458
H(7B)	−0.012	0.348	0.733	0.1458
H(8B)	−0.035	0.424	0.649	0.1458
H(9)	−0.603(3)	0.022(2)	0.088(1)	0.042(1)
H(10)	−0.611(3)	−0.091(2)	0.218(2)	0.042(1)
H(11)	−0.693(3)	0.075(2)	0.356(1)	0.042(1)
H(12)	−0.730(3)	0.287(2)	0.318(2)	0.042(1)

(continued)

TABLE 2 (continued)

Atom	x/a	y/b	z/c	U(equiv.) or U(iso)
H(13)	−0.673(3)	0.259(2)	0.143(2)	0.042(1)
H(14)	−0.057(3)	−0.030(1)	0.361(2)	0.042(1)
H(15)	0.164(3)	0.049(2)	0.492(2)	0.042(1)
H(16)	0.260(2)	0.281(2)	0.556(1)	0.042(1)
H(17)	0.121(3)	0.435(1)	0.485(2)	0.042(1)
H(18)	−0.090(3)	0.352(2)	0.348(2)	0.042(1)
H(19)	−0.015(2)	0.108(2)	0.173(2)	0.042(1)
H(20)	0.044(2)	0.172(2)	0.045(2)	0.042(1)
H(21)	−0.131(3)	0.285(2)	−0.047(1)	0.042(1)
H(22)	−0.372(2)	0.305(2)	−0.017(2)	0.042(1)
H(23)	−0.431(2)	0.230(2)	0.103(2)	0.042(1)
H(24)	−0.223(3)	−0.094(2)	0.067(2)	0.042(1)
H(25)	−0.357(3)	−0.117(2)	0.308(1)	0.042(1)
H(26)	−0.375(3)	−0.347(2)	0.252(2)	0.042(1)
H(27)	−0.306(3)	−0.459(1)	0.106(2)	0.042(1)
H(28)	−0.236(3)	−0.330(2)	0.012(1)	0.042(1)
H(29)	−0.452(3)	−0.137(2)	0.593(2)	0.042(1)

was used for the hydrogen atoms. The hydrogen atoms attached to C(4) and C(5A) and C(5B) were placed geometrically and given a temperature factor 1.2 times that of the atom to which they were bonded. During the final stages of refinement an extinction correction was applied [13]. The refinement was terminated when all shifts were less that 0.1σ with $R = 0.030$ ($R_w = 0.039$). The weight for each reflection was calculated from the Chebyshev series $w = [440.9\ t_0(X) + 598.4t_1(X) + 170.3t_2(X)]$ where $X = F_0/F_{max}$ [14]. All calculations were performed with the CRYSTALS package [15] on the Chemical Crystallography Laboratory VAX 11/750 computer. Final atomic positional coordinates with e.s.d.'s in parentheses are listed in Table 2. Selected bond lengths and bond angles are given in Table 3. Tables of thermal

TABLE 3

SELECTED BOND LENGTHS (Å) AND ANGLES (°) AND TORSIONAL ANGLES (°) WITH E.S.D.'S IN PARENTHESES FOR *RR,SS*-[(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_2CH_3$)] (**4b**)

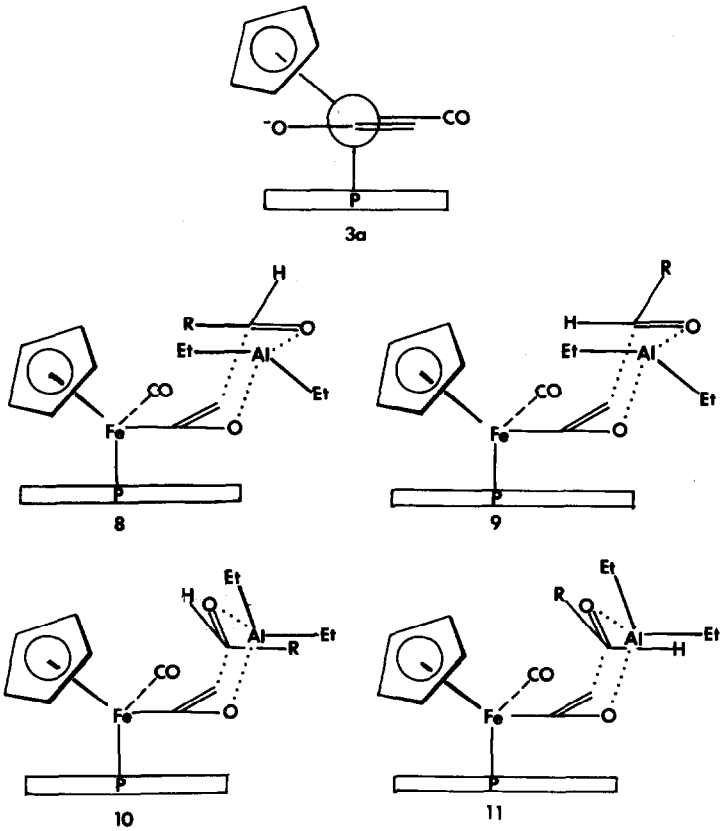
Fe(1)–P(1)	2.200(1)
Fe(1)–C(1)	1.963(2)
C(1)–O(1)	1.224(2)
C(1)–C(2)	1.530(2)
C(3)–O(2)	1.420(3)
C(1)–Fe(1)–C(6)	95.3(1)
C(1)–Fe(1)–P(1)	91.6(1)
P(1)–Fe(1)–C(6)	92.5(1)
Fe(1)–C(1)–O(1)	123.4(1)
Fe(1)–C(1)–C(2)	119.7(1)
C(6)–Fe(1)–C(1)–O(1)	169
C(1)–Fe(1)–P(1)–C(12)	34
Fe(1)–P(1)–C(12)–C(17)	67
C(1)–C(2)–C(3)–O(2)	67

parameters, structure factors, and a complete list of bond lengths and angles may be obtained from the authors.

Discussion

The aluminium enolate **3** smoothly undergoes aldol reactions with aldehydes. The enolate **3** is very nucleophilic showing little tendency to deprotonate enolisable aldehydes such as phenylacetaldehyde. The isolated yields for the β-hydroxyacyl complexes are high (85–90%) and these can be decomplexed to the corresponding β-hydroxy acids **6** and methyl esters **7**. In contrast to aldol reactions of the lithium enolate **2** high stereoselectivities are observed with the aluminium enolate **3**. Lower stereoselectivities are observed however if less than two equivalents of diethylaluminium chloride are added or if the enolate solutions are left for insufficient time at $-40°C$ for transmetallation to be completed.

Alkylation reactions of enolates bound to the $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ moiety occur only from the unhindered face, i.e. away from the blocking phosphine phenyl group, in the *anti*[O^-–CO] conformation [5]. The Newman projection of the *anti*-conformer of the enolate **3** is illustrated by **3a**. It can be seen from **3a** that the blocking phenyl group precludes approach of the aldehyde from the lower face of the enolate. Furthermore the space above and behind the enolate oxygen in **3a** is occupied by the sterically demanding cyclopentadienyl ligand whereas that above



the α-carbon of the enolate is sterically unencumbered. Assuming that the *anti*-conformation of the enolate is also the reactive conformation in these aldol reactions and that the aluminium promoted reactions occur via cyclic transition states then the two possible chair transition states are illustrated by **8** and **9**. Clearly in both **8** and **9** there will be severe steric interactions between the axial ethyl group on the aluminium and the cyclopentadienyl. For the two possible boat transition states **10** and **11** there are no unfavourable interactions with the cyclopentadienyl ligand. For transition state **10**, however, unfavourable 1,3-diaxial interactions between an aluminium ethyl group and the R group of the aldehyde will exist and therefore transition state **11** would be expected to be preferred. The relative stereochemistry of the newly formed chiral centre to the iron centre predicted from transition state **11** is consistent with that observed in these aldol reactions.

The above stereoselective reactions of the aluminium enolate derived from the iron acetyl complex **1** combined with known procedures for the resolution of **1** [16] will allow the development of efficient asymmetric syntheses of β-hydroxy carboxylic acids and derivatives based on the aldol and Reformatsky reactions.

Experimental

All reactions and purifications were performed under a nitrogen atmosphere using standard vacuum line and Schlenk tube techniques [17]. Tetrahydrofuran (THF) was dried over sodium benzophenone ketyl and distilled. Infrared spectra were recorded as Nujol mulls on a Perkin–Elmer 297 instrument. NMR spectra were recorded in $CDCl_3$ on Bruker WH 300 (300.13 MHz ^1H) and Bruker AM250 (62.896 MHz ^{13}C) spectrometers. Mass spectra were recorded on a V.G. Micromass ZAB 2F instrument using FD techniques. Elemental analyses were performed by Dr. F.B. Strauss, Oxford. n-Butyllithium (1.5 *M* in hexane) and diethylaluminium chloride (1.8 *M* in toluene) were used as supplied by Aldrich. The complex [(η^5-C_5H_5)Fe(CO)(PPh_3)COMe)] (**1**) was prepared according to the literature method [18].

Reaction of the lithium enolate 2 with aldehydes

n-BuLi (0.9 ml, 1.35 mmol) was added to an orange solution of the acetyl complex **1** (500 mg, 1.10 mmol) in THF at −78°C and the resulting dark-red mixture stirred at −78°C for 30 min. A solution of propanal (0.20 g, 3.44 mmol) in THF (10 ml) was added dropwise (15 min). After stirring at −78°C for a further 2 h methanol (1 ml) was added and the solution warmed to 20°C. Evaporation of the solvent and addition of dichloromethane (10 ml) gave a yellow solution. Filtration through alumina (Grade V) with ethyl acetate and evaporation gave **4b** and **5b** as a 1.2/1 mixture.

The results for the aldehydes MeCHO, $PhCH_2CHO$, i-PrCHO, t-BuCHO and PhCHO are given in Table 1.

Reaction of the aluminium enolate 3 with aldehydes

n-BuLi (0.9 ml, 1.35 mmol) was added to an orange solution of the acetyl complex **1** (310 mg, 0.68 mmol) in THF at −78°C and the resulting dark-red mixture was stirred at −78°C for 45 min. Diethyl aluminium chloride (2 ml, 3.6 mmol) was added to the reaction mixture which was warmed to −40°C and stirred

for 45 min. The mixture was cooled to −100°C and a solution of propanal (0.5 g, 8.62 mmol) in THF (10 ml) was added dropwise (5 min). After stirring at −100°C for 2 h, methanol (1 ml) was added and the solution warmed (20°C). Evaporation of the solvents, addition of dichloromethane (20 ml) and washing with sat. aq. $NaHCO_3$ (50 ml) gave a yellow solution. Filtration through alumina (Grade I, deactivated with 4% water) with diethyl ether to remove any small amounts of **1** present then ethyl acetate gave **4b** and **5b** as a > 100/1 mixture after evaporation.

The results for the aldehydes MeCHO, $PhCH_2CHO$, i-PrCHO, t-BuCHO and PhCHO are given in Table 1.

(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_3$) (3a). Found: C, 67.51; H, 5.62; P, 6.18. $C_{28}H_{27}FeO_3P$ calcd.: C, 67.49; H, 5.46; P, 6.22%; ν_{max} 3450br (OH), 1915vs (C≡O), 1585s (C=O) cm^{-1}; ^1H NMR δ 7.55–7.33 (15H, m, Ph), 4.44 (5H, d, *J*(PH) 1.2 Hz, C_5H_5), 3.49 (1H, d, *J* 0.7 Hz, O*H*), 3.29 (1H, m, C*H*), 2.88, 2.76 (2H, *ABX* system *J*(*AB*) 17.6 Hz, CH_2) 0.80 (3H, d, *J* 6.2 Hz, CH_3); ^{13}C {^1H} NMR δ 220.2 (d, *J*(PC) 31.0 Hz, C≡O), 136.2 (d, *J*(PC) 43.0 Hz, Ph C_{ipso}), 133.3 (d, *J*(PC) 9.5 Hz, Ph C_{ortho}), 129.9 (s, Ph C_{para}) 128.1 (d, *J*(PC) 10.2 Hz, Ph C_{meta}), 85.6 (s, C_5H_5), 73.8 (d, *J*(PC) 5.1 Hz, CH_2), 65.0 (s, C*H*), 21.3 (s, CH_3); *m/z* 498.

(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_2CH_3$) (3b). Found: C, 68.14; H, 5.59; P, 5.84. $C_{29}H_{29}FeO_3P$ calcd.: C, 67.98; H, 5.71; P, 6.05%; ν_{max} 3520br (OH), 1925vs (C≡O), 1585s (C=O) cm^{-1}; ^1H NMR δ 7.56–7.33 (15H, m, Ph), 4.44 (5H, d, *J*(PH) 1.1 Hz, C_5H_5), 3.44 (1H, d *J* 2.0 Hz, O*H*), 3.04 (1H, m, C*H*OH), 2.92, 2.76 (2H, *ABX* system *J*(*AB*) 17.5 Hz, CH_2CO), 1.27–1.00 (2H, m, CH_2CH_3), 0.74 (3H, t *J* 7.4 Hz, CH_3); ^{13}C {^1H} NMR δ 220.4 (d, *J*(PC) 30.1 Hz, C≡O), 136.1 (d, *J*(PC) 43.0 Hz, Ph C_{ipso}), 133.2 (d, *J*(PC) 9.8 Hz, Ph C_{ortho}), 129.8 (s, Ph C_{para}), 128.0 (d, *J*(PC) 10.0 Hz, Ph C_{meta}), 85.5 (s, C_5H_5, 71.8 (d, *J*(PC) 4.8 Hz, CH_2CO), 70.0 (s, C*H*OH), 28.3 (s, CH_2CH_3), 9.7 (s, CH_3); *m/z* 512.

(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH_2Ph$) (3c). Found: C, 71.42; H, 5.76; P, 5.10. $C_{34}H_{31}FeO_3P$ calcd.: C, 71.09; H, 5.44; P, 5.39%; ν_{max} 3360br (OH), 1915vs (C≡O), 1580s (C=O) cm^{-1}; ^1H NMR δ 7.53–7.05 (20H, m, Ph), 4.43 (5H, d, *J*(PH) 1.2 Hz, C_5H_5), 3.46 (1H, d, *J* 2.5 Hz, O*H*), 3.38 (1H, m, C*H*OH), 2.92, 2.85 (2H, *ABX* system *J*(*AB*) 17.5 Hz, CH_2CO), 2.50, 2.30 (2H, *ABX* system *J*(*AB*) 12.5 Hz, CH_2Ph); ^{13}C {^1H} NMR δ 220.1 (d, *J*(PC) 32.0 Hz, C≡O), 138.9 (s, CH_2Ph C_{ipso}), 136.1 (d, *J*(PC) 44.4 Hz, PPh_3 C_{ipso}) 133.2 (d, *J*(PC) 9.3 Hz, PPh_3 C_{ortho}), 129.8 (s, PPh_3 C_{para}), 129.2 (s, CH_2Ph C_{meta}), 128.2 (d, *J*(PC) 9.1 Hz, PPh_3 C_{meta}) 128.1 (s, CH_2Ph C_{ortho}), 126.0 (s, CH_2Ph C_{para}), 71.5 (d, *J*(PC) 6.8 Hz, CH_2CO), 69.8 (s, C*H*OH), 42.3 (s, CH_2Ph); *m/z* 574.

(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)CH(CH_3)_2$) (3d). Found: C, 68.38; H, 5.96; P, 5.55. $C_{30}H_{31}FeO_3P$ calcd.: C, 68.45; H, 5.94; P, 5.88%; ν_{max} 3520br (OH), 1915vs (C≡O), 1580s (C=O) cm^{-1}; ^1H NMR δ 7.58–7.32 (15H, m, Ph), 4.44 (5H, d, *J*(PH) 1.1 Hz, C_5H_5), 3.37 (1H, d, *J* 1.7 Hz, O*H*), 2.95–2.72 (3H, m, CH_2CHOH), 1.38–1.17 (1H, m, $CH(CH_3)_2$), 0.75 (3H, d, *J* 6.7 Hz, CH_3), 0.71 (3H, d, *J* 6.8 Hz, CH_3); ^{13}C {^1H} NMR δ 220.2 (d, *J*(PC) 30.1 Hz, C≡O), 136.2 (d, *J*(PC) 42.8 Hz, Ph C_{ipso}), 133.3 (d, *J*(PC) 10.5 Hz, Ph C_{ortho}), 129.8 (s, Ph C_{para}), 128.1 (d, *J*(PC) 9.5 Hz, Ph C_{meta}), 85.5 (s, C_5H_5), 73.2 (s, CHOH), 69.6 (d, *J*(PC) 5 Hz, $COCH_2$), 32.4 (s, $CH(CH_3)_2$), 18.4 (s, CH_3), 18.0 (s, CH_3); *m/z* 526.

(η^5-C_5H_5)Fe(CO)(PPh_3)($COCH_2CH(OH)C(CH_3)_3$) (3e). Found: C, 69.05; H, 6.33; P, 5.84. $C_{31}H_{33}FeO_3P$ calcd.: C, 68.90; H, 6.15; P, 5.73%; ν_{max} 3510br (OH), 1920vs (C≡O); 1580s (C=O) cm^{-1}; ^1H NMR δ 7.58–7.33 (15H, m, Ph), 4.45 (5H, d,

J(PH) 1.2 Hz, C_5H_5), 3.32 (1H, s, O*H*), 3.03 (1H, m, C*H*OH), 2.90, 2.75 (2H, *ABX* system *J*(*AB*) 10.5 Hz), 0.72 (9H, s, $(CH_3)_3$); ^{13}C {^1H} NMR δ 220.2 (d, *J*(PC) 30.5 Hz, *C*≡O), 136.3 (d, *J*(PC) 42.9 Hz, Ph C_{ipso}), 133.3 (d, *J*(PC) 10.0 Hz, Ph C_{ortho}), 129.8 (s, Ph C_{para}), 128.1 (d, *J*(PC) 9.4 Hz, Ph C_{meta}), 85.4 (s, C_5H_5), 75.4 (s, *C*HOH), 67.8 (d, *J*(PC) 4.7 Hz, *C*OCH_2), 33.5 (s, *C*$(CH_3)_3$) 25.8 (s, C(*C*$H_3)_3$); *m/z* 540.

(η^5-C_5H_5)Fe(CO)(PPh$_3$)(COCH$_2$CH(OH)Ph) (3f). ν_{max} 3460br (OH), 1920vs (C≡O), 1570s (C=O) cm^{-1}; ^1H NMR δ 7.60-7.11 (20 H, m, Ph). 4.42 (5 H, d, *J*(PH) 1.3 Hz, C_5H_5), 4.26–3.00 (3H, m, CH_2C*H*OH), 3.98 (1H, d, *J* 2.3 Hz, O*H*); ^{13}C {^1H} NMR δ 219.9 (d, *J*(PC) 31.7 Hz, *C*≡O), 143.6 (s, CH(OH)Ph C_{ipso}), 136.1 (d, *J*(PC) 44.4 Hz, PPh_3C_{ipso}), 133.3 (d, *J*(PC) 9.3 Hz, PPh_3 C_{ortho}), 129.9 (s, PPh_3 C_{para}), 128.3 (s, CH(OH)Ph C_{meta}), 128.1 (d *J*(PC) 9.3 Hz, PPh_3 C_{meta}), 126.6 (s, CH(OH)Ph C_{ortho}), 125.6 (s, CH(OH)Ph C_{para}), 85.5 (s, C_5H_5), 73.6 (s, *C*H_2), 71.1 (s, *C*HOH); *m/z* 560.

Decomplexations of β-hydroxy acyl complexes 3 to β-hydroxy acids 6

Complex **3e** (1.05 g, 1.94 mmol) and bromine (excess) were stirred together in a mixture of THF (30 ml) and water (0.2 ml) for 1 h at 20°C. On addition of sat. aq. $Na_2S_2O_3$ (2 ml) the orange suspension turned green. The organic solvent was removed under reduced pressure and sat. aq. $NaHCO_3$ (20 ml) added. The green solid was removed by filtration, dissolved in dichloromethane and filtered through alumina (Grade V) to give, after evaporation, (η^5-C_5H_5)Fe(CO)(PPh_3)Br (677 mg, 72%) identified by comparison with an authentic sample. The aqueous filtrate was acidified with 6 *N* HCl to pH 2, saturated with sodium chloride, extracted with diethyl ether (5 × 20 ml) and the combined extracts dried over Na_2SO_4. Filtration and evaporation gave crystalline **6e** (270 mg, 97%). The β-hydroxy acyl complexes **3b** and **3f** under similar conditions gave **6b** (69%) and **6f** (54%).

3-Hydroxypentanoic acid (6b). ^1H NMR δ 3.98 (1H, m, C*H*OH), 2.56, 2.46 (2H, *ABX* system, *J*(*AB*) 15.9, *J*(*AX*) 3.1, *J*(*BX*) 8.5 Hz, CH_2CO_2H), 1.54 (2H, m, CH_2CH_3), 0.94 (3H, t *J* 7.4 Hz, CH_2CH_3).

3-Hydroxy-4,4-dimethylpentanoic acid (6e). ^1H NMR δ 3.74 (1H, d, *J* 10.5 Hz, C*H*OH), 2.58, 2.42 (2H, *ABX* system *J*(*AB*) 16.2, *J*(*AX*) 0, *J*(*BX*) 10.7 Hz, CH_2CO_2H), 0.93 (9H, s, C(C$H_3)_3$).

3-Hydroxy-3-phenylpropionic acid (6f). ^1H NMR δ 7.62–7.10 (5H, m, Ph), 4.98 (1H, dd, *J* 9.5, 4.5 Hz), 2.62, 2.56 (2H, *ABX* system *J*(*AB*) 16.2, *J*(*AX*) 5.0, *J*(*BX*) 10.2 Hz, CH_2CO_2H).

Decomplexations of β-hydroxyacyl complexes 3 to the methyl esters 7

Complex **3b** (0.92 g, 1.80 mmol) and bromine (excess) were stirred together in a mixture of dichloromethane (30 ml) and anhydrous methanol (2 ml) for 1 h. On addition of sat. aq. $Na_2S_2O_3$ (5 ml) the orange suspension turned green. The organic solvents were removed under reduced pressure and the green residue triturated with 2 *N* NaOH (2 × 10 ml) and hot water (4 × 10 ml). The combined aqueous solutions were acidified with 6 *N* HCl to pH 2, saturated with sodium chloride and extracted with diethyl ether (6 × 10 ml) and ethyl acetate (2 × 10 ml). Drying over Na_2SO_4 and evaporation gave the ester **7b** (200 mg, 94%) as an oil.

Decomplexation, under the same conditions, of complexes **3a**, **3c**, **3d** and **3f** gave the methyl esters **7a** (81%), **7c** (62%), **7d** (86%) and **7f** (82%).

Methyl-3-hydroxybutanoate (7a). ^{1}H NMR δ 4.16 (1H, m, C*H*OH), 3.68 (3H, s, CO_2CH_3), 2.46, 2.41 (2H, *ABX* system *J*(*AB*) 16.4, *J*(*AX*) 4.2, *J*(*BX*) 8.2 Hz, CH_2), 1.20 (3H, d, *J* 6.3 Hz, CH_3).

Methyl-3-hydroxypentanoate (7b). ^{1}H NMR δ 3.91 (1H, m, C*H*OH), 3.68 (3H, s, CO_2CH_3), 2.49, 2.39 (2H, *ABX* system *J*(*AB*) 16.3, *J*(*AX*) 3.3, *J*(*BX*) 8.9 Hz, CH_2CO_2Me), 1.49 (2H, m, CH_2CH_3), 0.93 (3H, t, *J* 7.5 Hz, CH_2CH_3).

Methyl-3-hydroxy-4-phenylbutanoate (7c). ^{1}H NMR δ 7.40–7.20 (5H, m, Ph), 4.27 (1H, m, C*H*OH), 3.69 (3H, s, CO_2CH_3), 2.87, 2.77 (2H, *ABX* system *J*(*AB*) 13.6, *J*(*AX*) 6.2, *J*(*BX*) 7.1 Hz, $PhCH_2$), 2.52, 2.46 (2H, *ABX* system, *J*(*AB*) 16.4, *J*(*AX*) 4.0, *J*(*BX*) 8.4 Hz, $CH_2CO_2CH_3$).

Methyl-3-hydroxy-4-methylpentanoate (7d). ^{1}H NMR δ 3.77 (1H, ddd, *J* 3, 6, 9 Hz, C*H*OH), 3.70 (3H, s, CO_2CH_3), 2.49, 2.40 (2H, *ABX* system *J*(*AB*) 16.2, *J*(*AX*) 3.0, *J*(*BX*) 9.4 Hz, $CH_2CO_2CH_3$), 1.69 (1H, octet, *J* 6.6 Hz, $CH(CH_3)_2$), 0.93 (3H, d, *J* 6.9 Hz, $CH(CH_3)_2$), 0.90 (3H, d, *J* 7.0 Hz, $CH(CH_3)_2$).

Methyl-3-hydroxy-3-phenylpropionate (7f). ^{1}H NMR δ 7.50–7.25 (5H, m, Ph), 5.14 (1H, dd, *J* 8.7, 4.1 Hz), 3.72 (3H, s, CO_2CH_3), 2.77, 2.72 (2H, *ABX* system *J*(*AB*) 16.5, *J*(*AX*) 4.2, *J*(*BX*) 8.7 Hz).

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