Tetrahedron Vol 46 Nos 13/14, pp 4847-4856, 1990
Printed in Great Britain

0040-4020/90 $3.00 + .00

Asymmetric Synthesis of 2,4-Disubstituted Butyrolactones Using the Iron Chiral Auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$

Stephen G. Davies*, Robert Polywka and Peter Warner

The Dyson Perrins Laboratory, South Parks Road, Oxford, OX1 3QY, U.K.

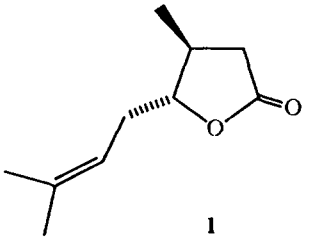
Dedicated to Professor W.D. Ollis on the occassion of his sixty-fifth birthday.

(*Received in UK 12 March 1990*)

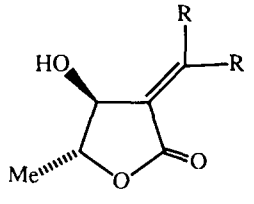
Summary: Treatment of the lithium enolate derived from homochiral S-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_3]$ with homochiral R- or S-propylene oxide or R-styrene oxide in the presence of diethylaluminium chloride followed by oxidative decomplexation generated *cis*-2S,4R-dimethyl butyrolactone, *trans*-2S,4S-dimethyl butyrolactone and *cis*-2S,4S-2-methyl-4-phenyl butyrolactone respectively. An X-ray crystal structure of the latter compound established unambiguously the relative and absolute configurations. Treatment of the lithium enolate from homochiral R-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_3]$ with R-styrene oxide in the presence of diethylaluminium chloride followed by oxidative decomplexation generated *trans*-2R,4S-2-methyl-4-phenyl butyrolactone. In the presence of diethylaluminium chloride the enolate from S-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_3]$ with racemic styrene oxide exhibited chiral discrimination in favour of the R-epoxide to the extent of >100:1.

Introduction:

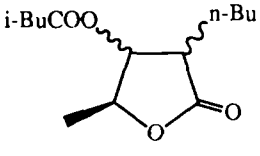
The butyrolactone (dihydro-(3H)-furanone) functionality is widespread throughout various natural product families,[1] and is also an integral moiety in a large number of molecules with important pharmacological applications.[2] The existence of several metabolites having as a constituent unit the butyrolactone ring such as eladonolide **1**, litsenolides **2**, and antimycinones **3** has generated an enormous interest in the synthesis and configurational assignments of various di- and tri-substituted butyrolactones. There has also been great interest in the molecular mechanics of simple butyrolactone systems geared towards configurational assignment.[3,4,5]



1

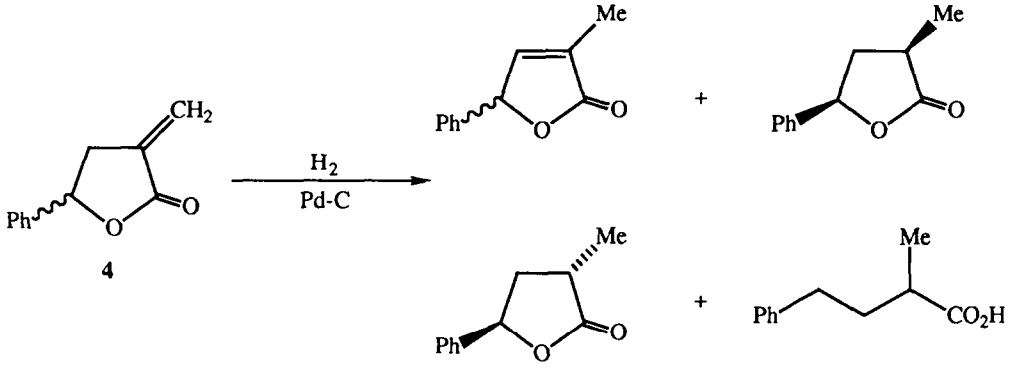


2

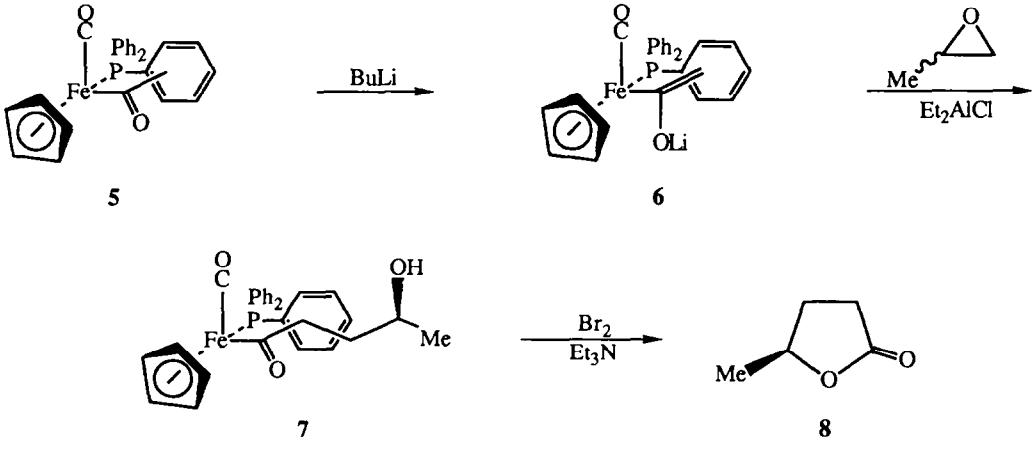


3

To date the most popular method for the synthesis of simple 2,4-disubstituted butyrolactones involves the stereoselective hydrogenation of a 4-substituted-2-*exo*-alkylidene butyrolactone, for example **4**.[3,6] The disadvantages of this method are the lengthy synthesis of compounds of type **4**, the mixture of products which then require separation and, unless the lactone **4** is homochiral, the resulting butyrolactones will be racemic.



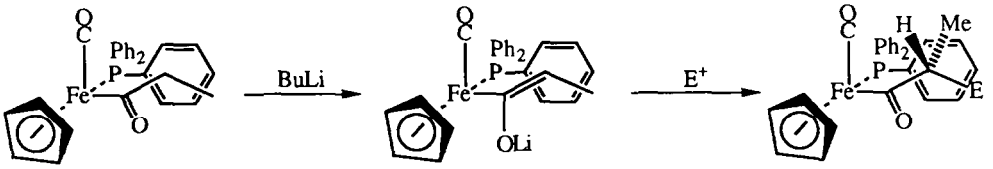
We have recently demonstrated that the lithium enolate derived from the parent chiral iron acetyl complex $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ (**5**) undergoes reactions with racemic monosubstituted epoxides in the presence of diethylaluminium chloride with high degrees of chiral recognition, the products of which can be decomplexed to butyrolactones.[7] For example, the enolate derived from racemic **5** reacts with racemic propylene oxide, in the presence of diethylaluminium chloride, to give **7** as a single diastereoisomer, thereby indicating that each enolate enantiomer reacts exclusively with only one epoxide enantiomer. The relative configurations within complex **7** were established by X-ray crystal structure analysis as RS(SR). Oxidative decomplexation of **7** produced the 4-methyl butyrolactone **8** efficiently.[7]



We report herein the extension of this methodology to the asymmetric synthesis of *cis*- and *trans*-2,4-disubstituted butyrolactones.

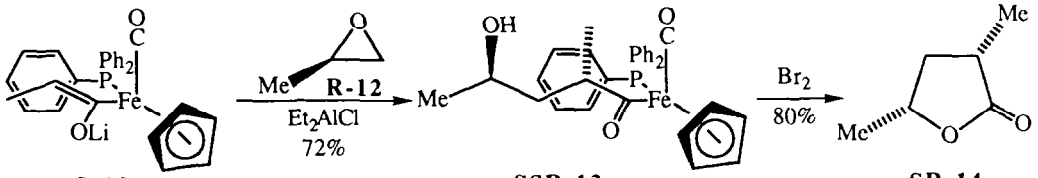
Results and Discussion

It has been previously established that deprotonation of the propanoyl complex **9** with butyllithium gives the E-enolate **10**, which reacts with electrophiles completely stereoselectively from the unhindered face in the conformation with the enolate oxygen *anti* to the carbon monoxide, to generate exclusively diastereoisomer **11**.[8]



9 **10** **11**

Deprotonation of the homochiral complex S-**9** with butyllithium generated the lithium enolate S-**10**. Addition of R-propylene oxide[9] (R-**12**) to the enolate S-**10** followed by diethylaluminium chloride gave, after work-up, the γ-hydroxy acyl complex **13**. The configurations within **13** were assigned as SSR‡ on the following basis. Since the S_N2 opening of the R-propylene oxide by the S-enolate must proceed without affecting either of the original chiral centres, the iron and γ-centres in **13** may be assigned as S and R respectively. The newly formed α-centre may be assigned as S and the basis of the characteristic ^{1}H n.m.r. chemical shift of the α-methyl doublet (δ 0.27). For α-methyl acyl complexes the α-methyl doublet appears at δ 0.1 - 0.5 for the RR(SS) diastereoisomers, but at δ 0.8 - 1.3 for the RS(SR) diastereoisomers.[10] Complex **13** was produced completely stereoselectively according to ^{1}H n.m.r. spectroscopic analysis consistent with both the propanoyl complex S-**9** and the R-propylene oxide being homochiral and with the formation of the new α-chiral centre being completely stereoselective.

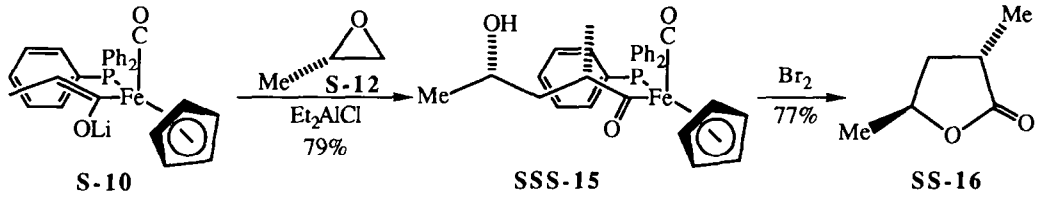


S-10 **SSR-13** **SR-14**

Decomplexation of SSR-**13** with bromine gave *cis*-2S,4R-dimethyl butyrolactone (**14**). Since SSR-**13** is homochiral it follows that SR-**14** is also homochiral. The structure and configuration of **14** were assigned on the basis of the established configuration of SSR-**13**, with the assumption that lactone formation had occurred with retention at the 4-position and without epimerisation at the 2-position.

‡ Configurations are listed in order starting at the iron centre.

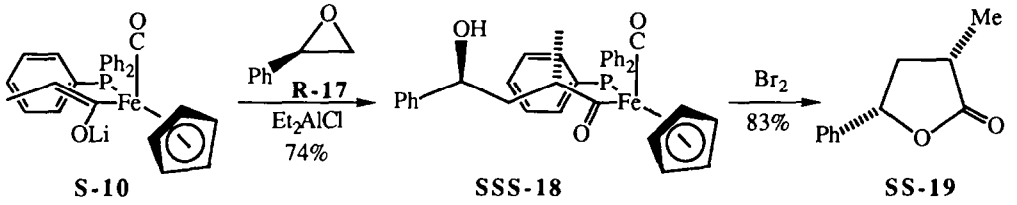
Treatment of the lithium enolate S-**10** with homochiral S-proylene oxide[11] (S-**12**) generated, in the presence of diethylaluminium chloride, completely stereoselectively, SSS-**15**. The configurations of **15** were assigned on the same basis as for SSR-**13**, the α-methyl doublet appearing at δ 0.26 in the ^{1}H n.m.r. spectrum. Oxidative decomplexation of SSS-**15** gave *trans*-2S,4S-dimethyl butyrolactone SS-**16**.



S-**10** SSS-**15** SS-**16**

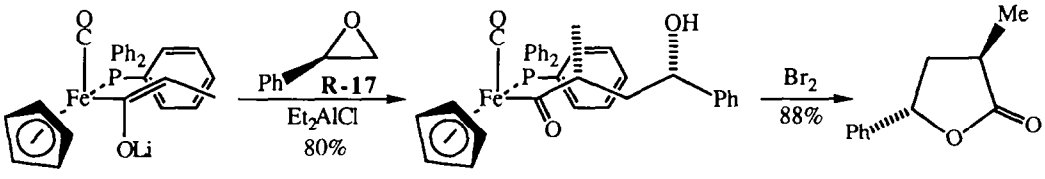
Ollis *et. al.* have previously reported the preparation of racemic samples of the *cis*- and *trans*-2,4-dimethyl butyrolactones **14** and **16**.[3] Our ^{1}H n.m.r spectroscopic data for the homochiral compounds SR-**14** and SS-**16** agrees with their data for the racemates and validates our assumptions concerning the stereospecificity of the lactone formation step.

Treatment of the lithium enolate S-**10** with homochiral R-styrene oxide (R-**17**) in the presence of diethylaluminium chloride generated SSS-**18** as a single diastereoisomer (α-methyl doublet δ 0.36). Oxidative decomplexation gave *cis*-2S,4S-2-methyl-4-phenyl butyrolactone (SS-**19**).



S-**10** SSS-**18** SS-**19**

Generation of the lithium enolate R-**10** by deprotonation of homochiral R-**9**, followed by treatment with R-**17** and diethylaluminium chloride gave RRS-**20** completely stereoselectively (α-methyl doublet at δ 0.39). Decomplexation of RRS-**20** gave *trans*-2R,4S-2-methyl-4-phenyl butyrolactone (RS-**21**).



R-**10** RRS-**20** RS-**21**

Comparison of our spectroscopic data for SS-**19** and RS-**21** with that in the literature[3] for the corresponding racemates is consistent with our configurational assignments. Previous structural assignments for *cis*- and *trans*-2,4-disubstituted butyrolactones have been based on the chemical shifts and coupling constants of the 3-methylene protons. In particular a relatively large chemical shift difference between the 3-methylene

protons was taken as indicative of the *cis*-relationship of the 2- and 4-substituents. Chemical shift data and coupling constants for the compounds SR-**14**, SS-**16**, SS-**19** and RS-**21** are listed in Table 1.

Table 1: Selected ^{1}H NMR Chemical Shift and Coupling Constant Data for 2,4-Disubstituted Butyrolactones

	Chemical Shift (δ)		Coupling Constants (Hz)				
	$H_{3\alpha}$	$H_{3\beta}$	$H_2H_{3\alpha}$	$H_2H_{3\beta}$	$H_{3\alpha}H_{3\beta}$	$H_{3\alpha}H_4$	$H_{3\beta}H_4$
SR-**14**	2.6-2.68	1.28-1.60	8.4	12.4	12.2	6.0	11.0
SS-**16**	1.95-2.1	1.95-2.1	8.1	8.9	--*	7.0	7.4
SS-**19**	2.85	1.80	8.2	12.2	12.2	5.7	10.8
RS-**21**	2.45	2.45	7.1	8.6	--*	7.4	5.5

* The similarity in chemical shifts for H_α, and H_β did not allow this coupling to be determined.

The X-ray crystal structure for SS-**19** is shown in the Figure and confirms unambiguously the *cis* stereochemistry. Furthermore, a Flack enantiopole refinement (0.73) was consistent with the assigned SS-absolute stereochemistry. Final atomic positional coordinates for SS-**19** are listed in Table 2. Selected torsional angles are given in Table 3.

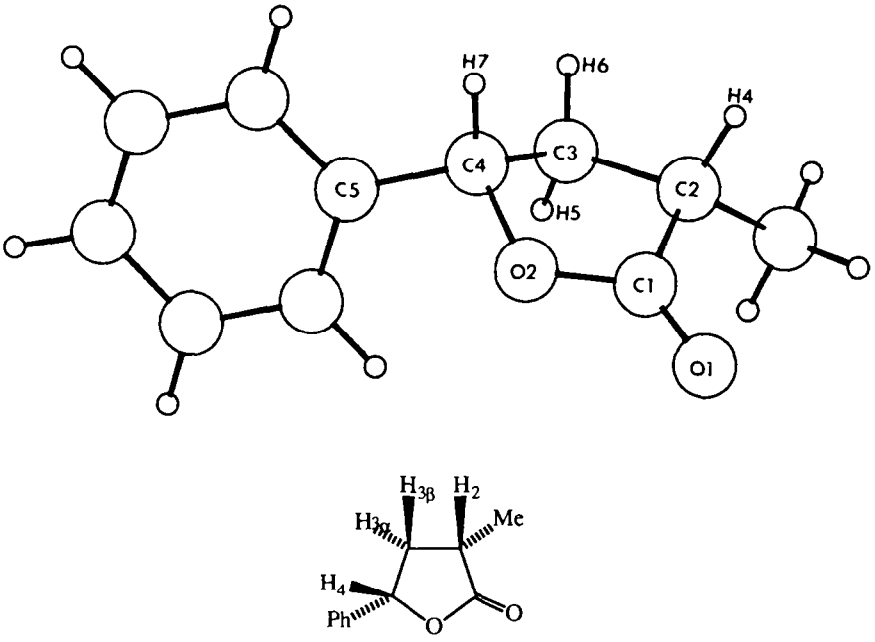


Figure: X-Ray Crystal Structure of *cis*-2S,4S-2-Methyl-4-phenyl Butyrolactone (SS-**19**).

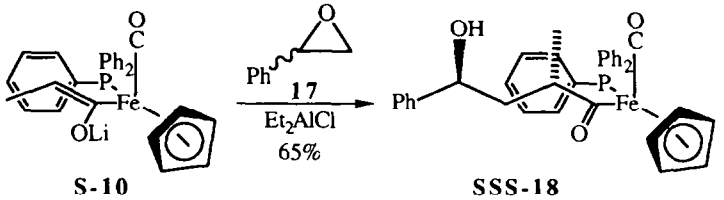
Table 2 Final Atonic Coordinates for *cis*-2S,4S-2-Methyl-4-phenyl Butyrolactone **(19)**

Atom	x/a	y/b	z/c	U(iso)
C (1)	0.1491 (8)	0.1262 (7)	0.5026 (6)	0.0666
C (1)	0.2923 (8)	0.1914 (6)	0.3884 (5)	0.0636
C (3)	0.4531 (8)	0.2913 (6)	0.4805 (5)	0.0635
C (4)	0.4794 (8)	0.2076 (6)	0.6219 (5)	0.0606
C (5)	0.5342 (7)	0.2990 (6)	0.7518 (5)	0.0575
C (6)	0.7483 (8)	0.2895 (8)	0.8225 (5)	0.0743
C (7)	0.800 (1)	0.3801 (9)	0.9409 (6)	0.0904
C (8)	0.647 (1)	0.4764 (9)	0.9903 (6)	0.0899
C (9)	0.435 (1)	0.4876 (8)	0.9211 (7)	0.0872
C (10)	0.3799 (9)	0.4009 (6)	0.8021 (6)	0.0708
C (11)	0.155 (1)	0.2696 (7)	0.2667 (6)	0.0882
O (1)	-0.0366 (7)	0.0721 (6)	0.4855 (4)	0.0915
O (2)	0.2550 (5)	0.1373 (5)	0.6331 (3)	0.0639
H (1)	0.255 (1)	0.3110 (7)	0.1934 (6)	0.14 (2)
H (2)	0.068 (1)	0.3521 (7)	0.3099 (6)	0.14 (2)
H (3)	0.046 (1)	0.1970 (7)	0.2195 (6)	0.14 (2)
H (4)	0.3771 (8)	0.1191 (6)	0.3301 (5)	0.13 (3)
H (5)	0.3816 (8)	0.3901 (6)	0.4967 (5)	0.11 (2)
H (6)	0.6020 (8)	0.3060 (6)	0.4363 (5)	0.11 (2)
H (7)	0.6085 (8)	0.1362 (6)	0.6177 (5)	0.07 (1)
H (8)	0.8635 (8)	0.2197 (8)	0.7860 (5)	0.12 (1)
H (9)	0.954 (1)	0.3724 (9)	0.9908 (6)	0.12 (1)
H (10)	0.688 (1)	0.5368 (9)	1.0079 (6)	0.12 (1)
H (11)	0.323 (1)	0.5615 (8)	0.9549 (7)	0.12 (1)
H (12)	0.2265 (9)	0.4080 (6)	0.7515 (6)	0.12 (1)

Table 3: Selected Torsional Angles (°) for *cis*-2S,4S-2-Methyl-4-phenyl Butyrolactone **(19)**:

X-ray numbering		Systematic numbering
H (4) - C (2) - C (3) - H (6)	28.3	$H_2 - C_2 - C_3 - H_{3\alpha}$
H (4) - C (2) - C (3) - H (5)	150.9	$H_2 - C_2 - C_3 - H_{3\beta}$
H (6) - C (3) - C (4) - H (7)	-32.1	$H_{3\alpha} - C_3 - C_4 - H_4$
H (5) - C (3) - C (4) - H (7)	-153.7	$H_{3\beta} - C_3 - C_4 - H_4$
C (1) - C (2) - C (3) - C (4)	32.2	
C (2) - C (3) - C (4) - O (2)	-33.6	
C (3) - C (4) - C (5) - C (6)	-109.9	

Having established unambiguously the structures of the *cis*- and *trans*-2,4-disubstituted butyrolactones it was now possible to investigate whether any chiral recognition occurred in the reaction of enolate **10** with propylene and styrene oxides. In order to avoid the effects of mass action distorting the results, the chiral recognition experiments were performed initially on racemic materials. Treatment of racemic enolate **10** with racemic propylene oxide in the presence of boron trifluoride gave a 50:50 mixture of epimers **13** and **15** indicating a complete absence of chiral recognition, but still, as expected, with complete control over the configuration of the α-centre relative to the iron centre. In the presence of diethylaluminium chloride as Lewis acid a 75:25 mixture of **13** and **15** was formed indicating a preference of the R-enolate for the S-epoxide and consequently of the S-enolate for the R-epoxide. In the reactions of the racemic enolate **10** with racemic styrene oxide no chiral recognition was observed with boron trifluoride; epimers **18** and **20** were produced in equal amounts. However in the presence of diethylaluminium chloride only complex RRR(SSS)-**18** could be detected. This latter result indicated a very substantial preference of the R-enolate **9** for S-styrene oxide. The R-enolate prefers to react at least 100 times faster with S-styrene oxide than with R-styrene oxide. Treatment of the homochiral enolate S-**10** with an excess racemic styrene oxide and diethylaluminium chloride similarly generated SSS-**18** as a single diastereoisomer.



S-10 **SSS-18**

Experimental

All reactions and purifications were performed under nitrogen using standard vacuum line and Schlenk techniques.[12] Removal of all solvents carried out under reduced pressure. THF was dried over sodium benzophenone ketyl and distilled. Dichloromethane was distilled from calcium hydride. Diethylaluminium chloride was used as a 2.0 M solution in toluene, and n-butyllithium (1.4 M in hexane) was used as supplied by Aldrich. I.r. spectra were recorded in dichloromethane on a Perkin Elmer 297 instrument. Proton n.m.r. spectra were recorded on a Bruker WH 300 spectrometer at 300.13 MHz, using $CDCl_3$ as the solvent with chemical shifts being reported as δ ppm from $(CH_3)_4Si$. Carbon-13 n.m.r. spectra were recorded on a Bruker AM 250 spectrometer at 62.90 MHz using $CDCl_3$ as the solvent and internal standard and are reported as δ ppm from $(CH_3)_4Si$. Phosphorus-31 n.m.r. spectra were recorded at 101.26 MHz using $CDCl_3$ as solvent and are reported as δ ppm from an external reference of triethylphosphate in D_2O. Electron impact mass spectra were recorded on V.G. micromass ZAB 2F instrument using field desorption (FD) technique. Optical rotations were recorded on a Perkin-Elmer 241 polarimeter. Elemental analyses were performed by the Dyson Perrins Analytical Services (Oxford, U.K.). Homomchiral R- and S-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COC_2H_5]$ were supplied by Oxford Chirality .[13]

General Preparation of $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)(COCH(CH_3)CH_2CH(R)OH]$ *(R=Me, Ph).*- n-Butyllithium (1.2 eq.) was added to an orange solution of the propanoyl complex **9** (1.1 mmol), in THF (15 ml) at -78°C and the resulting deep red solution stirred at -78°C for 1 hr. The epoxide (1 eq.) and Lewis acid (3 eq.) were added and the solution stirred at -78°C for 6 hrs. The reaction was quenched with MeOH (1 ml). Work up when

Et_2AlCl was used as the Lewis acid involved removal of solvent under reduced pressure and extraction of the residue with dichloromethane (20 ml). When $BF_3.Et_20$ is the Lewis acid the reaction mixture was adsorbed onto alumina (Grade V). Column chromatography on flash silica eluting with Et_20 followed by evaporation of the solvent gave the product as a yellow/red foam.

Preparation of SSR-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH$_3$)CH$_2$CH(Me)OH] (**13**).- (Yield 72%); $[\alpha]_D^{20}$ +183.3 (c 0.08, CH_2Cl_2); υ_{max} 1910 (CO), 1600 (C=O) 3300 - 3500 (OH) cm^{-1}; ^1H n.m.r. δ 7.6 - 7.3 (15H, m, 3 x C_6H_5), 4.46 (5H, d, J_{P-H} 1.0 Hz, C_5H_5), 3.76 - 3.72 (1H, m, CHOH), 3.13 - 3.03 (1H, m, COCH), 1.91 (1H, ddd, ^2J 14H, J 10.1 Hz, 3.6 Hz, $COCH(CH_3)CH_2$), 1.57 (1H, d, J 5.3 Hz, OH), 1.21 (3H, d, J 6.2 Hz) $CH(CH_3)OH$), 1.05 (1H, ddd, ^2J 13.9 Hz, J 10.5, 2.5 Hz, $COCH(CH_3)CH_2$), 0.27 (3H, d, J 6.4 Hz, $COCH(CH_3)$; $^{13}C\{^1H\}$ n.m.r. δ281.3 (d, J_{P-C}, J 23 Hz C=O) 221.1 (d, J_{P-C} 31 Hz, CO), 136.5 (d, J_{P-C} 43 Hz, PPh_3 C_{ipso}), 133.3 (d, J_{P-C} 10 Hz, PPh_3 C_{ortho}), 129.6 (s, PPh_3 C_{para}), 127.9 (d, J_{P-C} 10 Hz, PPh_3, C_{meta}), 85.3 (s, C_5H_5), 65.8 (s, CHOH), 63.7 (d, J_{P-C} 5 Hz, COCH), 42.2 (s, CH_2), 24.7 (s, CH_3), 15.0 (s, CH_3). $^{31}P\{^1H\}$ n.m.r. δ 71.0 (s, PPh_3).

Preparation of SSS-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH$_3$)CH$_2$CH(Me)OH] (**15**).- (Yield 79%); $[\alpha]_D^{20}$ +228.0 (c 0.05, CH_2Cl_2); υ_{max} 1910 (CO), 1600 (C=O) 3300 - 3500 (OH) cm^{-1}; ^1H n.m.r. δ7.6 - 7.3 (15H, m, 3 x C_6H_5), 4.48 (5H, d, J 1.3 Hz, C_5H_5) 3.84 - 3.78 (1H, m, CH(OH), 3.13 - 3.03 (1H, m, COCH), 2.38 (1H, d, J 3.0 Hz, OH), 1.69 (1H, dt, ^2J 13.8 Hz, J 5.6 Hz, COCH (CH_3) CH_2), 1.45 (1H, ddd, ^2J 14.0 Hz, J 7.8 Hz, 6.3 Hz, COCH (CH_3) CH_2), 1.18 (3H, d, J 6.2 Hz, $CH(CH_3)OH$), 0.26 (3H, d, J 6.7 Hz, COCH CH_3); $^{13}C\{^1H\}$ n.m.r. δ 220.8 (d, J_{P-C} 31 Hz, CO), 136.6 (d, J_{P-C} 42.8 Hz, PPh_3 C_{ipso}), 133.3 Hz (d, J_{P-C}, J 10.0 Hz, PPh_3, C_{ortho}), 129.7 (s, PPh_3, C_{para}), 128.0 (d, J 10 Hz, PPh_3, C_{meta}), δ 85.4 (s, C_5H_5), 65.3 (s, CH(OH), 64.4 (d, J_{P-C} 5 Hz, COCH), 40.9 (s, CH_2), 23.4 (s, CH_3), 14.4 (s, CH_3). $^{31}P\{^1H\}$ n.m.r. δ 71.0 (s, PPh_3).

Preparation of SSS-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH$_3$)CH$_2$CH(Ph)OH] (**18**).- (Yield 74%); $[\alpha]_D^{20}$ +104.5 (c 0.09, CH_2Cl_2); υ_{max} 1910 (CO), 1600 (C=O) 3400 (OH) cm^{-1}; ^1H n.m.r. δ 7.6 - 7.1 (20H, m, 4 x C_6H_5), 4.63 (1H, ddd, J 10.5 Hz, 4.5, 2.9 Hz, CHOH), 4.44 (5H, s, C_5H_5), 3.20 (1H, qdd, J 6.5 Hz, 10.3, 3.78 Hz, $CHCH_3$), 2.23 (1H, ddd, ^2J 14.4 Hz, ^3J 10.3, 3.7 Hz CH_2), 2.15 (1H, d, J 4.7 Hz, OH), 1.29 (1H, ddd, ^2J 14.4 Hz, ^3J 10.4 Hz, 2.8 Hz, CH_2), 0.36 (3H, d, J 6.6 Hz, CH_3); $^{13}C\{^1H\}$ n.m.r. δ 281.7 (s, C=O), 221.0 (d, J_{P-C} 30 Hz, CO), 145.7 (s, C_6H_5, C_{ipso}), 136.4 (d, J_{P-C}42 Hz, PPh_3, C_{ipso}), 133.1 (d, J_{P-C}, J 9.7 Hz, PPh_3, C_{ortho}), 129.6 (s, PPh_3, C_{para}), 128.2 (s, C_6H_5 C_{ortho}), 127.8 (d, J 9.8 Hz, PPh_3, C_{meta}), 126.3 (s, C_6H_5, Cpara, 125.4 (s, C_6H_5, C_{meta}), 85.2 (s, C_5H_5), 72.0 (s, CHOH), 63.7 (d, J_{P-C} 5 Hz, $CH(CH_3)$, 42.4 (s, CH_2), 14.8 (s, CH_3); $^{31}P\{^1H\}$ δ71.2 (s, PPh_3).

Preparation of RRS-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH$_3$)CH$_2$CH(Ph)OH] (**20**).- (Yield 80%); $[\alpha]_D^{20}$ -165.0 (c 0.1, CH_2Cl_2); υ_{max} 1910 (CO), 1600 (C=O), 3400 (OH) cm^{-1}; ^1H n.m.r. δ 7.6 - 7.1 (20H, m, 4 x C_6H_5), 4.73 (1H, ddd, J 10.1 Hz, 4.6 Hz, 3.0 Hz, CHOH), 4.43 (5H, d, J_{P-H} 1.1 Hz, C_5H_5), 3.20 (2H, m, $CHCH_3$, CHOH), 1.95 - 1.80 (2H, m, CH_2), 0.39 (3H, d, J 6.5 Hz CH_3); $^{13}C\{^1H\}$ n.m.r. δ 220 (d, J_{P-C} 31 Hz, CO), 145.6 (s, C_6H_5, C_{ipso}), 136.4 (d, J_{P-C} 41 Hz, PPh_3, C_{ipso}), 133.1 (d, J_{P-C} 9.7 Hz, PPh_3, C_{ortho}), 129.5 (s, PPh_3, C_{para}), 128.0 (s, C_6H_5, C_{ortho}), 127.8 (d, J_{P-C} 9.8 Hz, PPh_3, C_{meta}), 126.0 (s, C_6H_5, C_{para}), 125.3 (s, C_6H_5, C_{meta}), 85.3 (s, C_5H_5), 72.1 (s, CH(OH), 63.8 (s, $CH(H_3)$, 42.5 (s, CH_2) 14.9 (s, CH_3); $^{31}P\{^1H\}$ n.m.r. δ 71.0 (s, PPh_3).

Mixtures of racemic **13** and **15**, and of racemic **18** and **20** were synthesised as for the homochiral analogues using boron trifluroride etherate as the Lewis acid. Satisfactory analytical and mass spectral data were

obtained for the mixtures: SSR(RRS)-**13** and SSS(RRR) **15** (Found C 68.8; H 6.05; P 6.0. $C_{30}H_{31}FeO_3P$ requires C 68.45; H 5.94; P 5.88 %); m/z 526: SSS(RRR)-**18** and RRS(SSR)-**20** (Found C 71.15; H 5.80; P, 5.0. $C_{35}H_{33}FeO_3P$ requires C 71.44; H 5.65; P 5.26 %); m/z 588. Separation into the component diastereoisomers was performed by flash chromatography eluting with Et_2O. The spectroscopic data was identical to those of the homochiral analogues.

General method for the decomplexation of α-methyl-γ-hydroxy iron complexes to 2,4-disubstituted butyrolactones.- A solution of the iron complex in THF was cooled to -78°C, Br_2(1.2 eq) was added and the resultant green solution allowed to stir at -78°C for 1 hr. Excess triethylamine was then added, and the solution then allowed to warm to ambient temperature. Removal of solvents under reduced pressure followed by extraction of the solid residue (Et_2O) resulted in a green solution. Standing in air for 3 days resulted in the precipitation of a brown solid; filtering through a small plug of flash silica gave a pale yellow solution, which on removal of the solvent gave the desired butyrolactone as a yellow oil. Final purification was performed by flash chromatography on Silica gel eluting with Et_2O.

cis-2S,4R-Dimethyl butyrolactone (**14**).- (Yield 80%); $[\alpha]_D^{20}$ +1.4 (c 1.0, CH_2Cl_2); υ_{max} ($CHCl_3$) 1763 cm^{-1} (C=O); ^1H n.m.r. δ 4.51 - 4.40 (1H, qdd, $J_{4,Me}$ 6.0 Hz, $J_{4,3\alpha}$ 6.0 Hz, $J_{4,3\beta}$ 11.0 Hz, H-4) 2.71 - 2.62 (1H, m, $J_{2,3\alpha}$ 8.4 Hz, $J_{2,3\beta}$ 12.4 Hz, H-2), 2.6 - 2.68 (1H, m, $H_{3\alpha}$), 1.28 - 1.6 (1H, ddd, $J_{3\beta,4}$ 11.0 Hz, $J_{3\beta,2}$ 12.4 Hz, $J_{3\alpha,3\beta}$ 12.2 Hz, $H_{3\beta}$), 1.36 (3H, d, J 6.2 Hz, Me-4), 1.23 (3H, d, J 6.9 Hz, Me-2); $^{13}C\{^1H\}$ δ 179.5 (s, C=O), 74.85 (s, CH), 53.39 (s, CH_2), 36.39 (s, CH), 20.95 (s, CH_3), 15.13 (s, CH_3).

trans-2S,4S-Dimethyl butyrolactone (**16**).- (Yield 77%); $[\alpha]_D^{20}$ +11.8 (c 2.05, CH_2Cl_2); υ_{max} ($CHCl_3$) 1760 cm^{-1} (C=O); ^1H n.m.r. ($CDCl_3$) δ 4.65 - 4.56 (1H, qdd, $J_{4,Me}$ 2.4 Hz, $J_{4,3\alpha}$ 7.0 hz, $J_{4,3\beta}$ 7.4 Hz, H-4) 2.68 - 2.58 (1H, qdd, $J_{2,Me}$ 7.4 Hz, $J_{2,3\alpha}$ 8.1 Hz, $J_{2,3\beta}$ 8.9 Hz, H-2), 1.95 -2.1 (2H, m, $H_{3\alpha,3\beta}$), 1.27 (3H, d, J 2.4 Hz, Me-4), 1.17 (3H, d, J 7.4 Hz, Me-2); $^{13}C\{^1H\}$ n.m.r. ($CDCl_3$) δ 179.75 (s, C=O), 74.50 (s, CH), 53.36 (s, CH_2), 34.03 (s, CH), 21.08 (s, CH_3), 15.75 (s, CH_3).

cis-2S,4S-2-Methyl-4-phenyl butyrolactone (**19**).- (Yield 83%); $[\alpha]_D^{20}$ -20.0 (c 4.65, CH_2Cl_2); υ_{max} ($CHCl_3$) 1760 cm^{-1} (C=O); ^1H n.m.r. δ 7.33 (5H, m, C_6H_5), 5.35 (1H, dd, $J_{4,3\alpha}$ 5.7 Hz, $J_{4,3\beta}$ 10.8 Hz, H-4) 2.85 (2H, m, $J_{2,3\alpha}$ 8.2 Hz, $J_{2,3\beta}$ 12.2 Hz, $H_{2,3\alpha}$), 1.80 (1H, ddd, $J_{3\beta,4}$ 10.8 Hz, $J_{3\beta,2}$ 12.2 Hz, $J_{3\beta,3\alpha}$ 12.2 Hz, $H_{3\beta}$), 1.85 (3H, d, J 6.6 Hz, CH_3); $^{13}C\{^1H\}$ n.m.r. δ 179.80 (s, C=O), 129.70 (s, C_5H_6, C_{ipso}), 128.73 (s, C_6H_5, C_{ortho}), 128.17 (s, C_6H_5, C_{para}), 124.96 (s, C_6H_5, C_{meta}), 78.3 (s, CH) 38.36 (s, CH_2), 33.57 (s, CH), 15.41 (s, CH_3).

X-ray Crystal Structure Analysis of cis-2S,4S-2-Methyl-4-phenyl Butyrolactone (**19**).- Cell parameters and intensity data were measured using graphite monochromated CuKα radiation on an Enraf Nonius CAD 4-F diffractometer operating in ω:2θ mode. The scan range ω was calculated from [0.8 + 0.15 tan θ] and the scan speed varied from 1.25 to 6.7° min^{-1} depending upon intensity. Reflections were measured in the range O<θ<72°. Three reflections were remeasured regularly throughout the data collection and were used to scale the data to correct for any crystal decay. The data were corrected for Lorentz, polarization and absorption effects[14] and equivalent reflections in the 2367 measured intensities were merged to give 1199 reflections of which 990 were considered to be observed [I>3σI] and were used in the subsequent structure analysis. The structure was solved by direct methods using SHELX S86.[15]

Full-matrix least-squares refinement was performed on all non-hydrogen atom postional and anisotropic thermal parameters an overall scale factor and the Flack enantiopole. Hydrogen atom positions were calculated based on idealised geometry and allowed to "ride" on the atom to which it was and isotropic thermal parameters

for each type of H-atom were included in the refinement. Unit weights were used throughout. At convergence rms shift/e.s.d. = 2 x 10^{-4} All calculations were performed using the CRYSTALS package on the Chemical Crystallography Laboratory Micro VAX-3 computer.

Crystal Data $C_{11}H_{12}O_2$, m = 176.2146 g, monoclinic, space group $P2_1$, a = 5.910(2), b = 9.005(2), c = 9.320(2) A, β = 93.31(3)° U = 495 A^3, Z=2, relative transmission factors 1.0-1.17, crystal dimensions 1.25 x 0.2 x 0.55 mm, number of reflections [I > 3 σ (I)] 990, R=0.058, R_w=0.052.

trans-2R,4S-2-Methyl-4-phenyl butyrolactone (**21**).- (Yield 88%); $[\alpha]_D^{20}$ +1.4 (c 1.6, CH_2Cl_2); υ_{max} ($CHCl_3$) 1760 cm^{-1} (C=O); ^1H n.m.r. δ 7.35 (5H, m, C_6H_5), 5.60 (1H, dd, $J_{4,3\alpha}$ 7.4 Hz, $J_{4,3\beta}$ 5.5 Hz, H-4), 2.75 (1H, qdd, $J_{2,Me}$ 7.2 Hz, $J_{2,3\alpha}$ 7.1 Hz, $J_{2,3\beta}$ 8.6 Hz, H-2), 2.45 (2H, m, $H_{3\alpha,\beta}$), 1.35 (3H, d, 7.2 Hz, CH_3); $^{13}C\{^1H\}$ n.m.r. δ 179.00 (s, C=O), 139.10 (s, C_6H_5, C_{ipso}), 128.65 (s, C_6H_5, C_{ortho}), 128.39 (s, C_6H_5, C_{para}), 125.41 (s, C_6H_5, C_{meta}), 79.09 (s, CH), 39.87 (s, CH_2), 36.28 (s, CH), 14.93 (s, CH_3).

*Reaction of the lithium enolate of S-[(η^5-C_5H_5)Fe(CO)(PPh_3)(COC_2H_5)] (**9**) with racemic styrene oxide (**17**).*- n-Butyllithium (0.6 ml, 0.76 mmol) was added to an orange solution of the propanoyl complex **9** (300 mg, 0.64 mmol), in THF (15 ml) at -78°C and the resulting deep red solution stirred at -78°C for 1 hr. Styrene oxide (0.07 ml, 3.18 mmol) and diethyl aluminium chloride (4.8 ml, 9.54 mmol) were added and the solution stirred at -78°C for 6 hrs. The reaction was quenched with MeOH (~ 1 ml). Removal of solvent under reduced pressure and extraction of the residue with dichloromethane (~ 20 ml) gave an orange oil which was chromatographed on flash silica eluting with Et_20. Evaporation of the solvent gave the product as a red solid. (Yield 240 mg, 65%). Spectroscopic data were consistent with diastereomerically pure SSS-**18**. $[\alpha]_D^{20}$ +113.1 (c 0.10, CH_2Cl_2).

Acknowledgements: We thank ICI Pharmaceuticals for a Studentship (to RP), the SERC for a Quota Award (to PW), Dr Keith Prout for access to the facilities of the Chemical Crystallography Department and Alison J. Edwards for help with the crystal structure determination.

References

1. K. Nakanishi, T. Goto, S. Ito and S. Nozoe, Natural Products Chemistry, Kodansha Ltd., Tokyo, 1974.
2. F.A. Levine, F.A. Ferrendelli and P.F. Corey, *J. Med. Chem.*, 1986, **29**, 1996.
3. S.M.A.T. Hussain, W.D. Ollis, D. Smith and J.F. Stoddart, *J.C.S. Perkin I*, 1975, 1480.
4. M.H.P. Guy, A.S. George and P.N.J. White, *J.C.S. Perkin I*, 1976, 1917.
5. C. Jaine, R.M. Ortuno, and J. Font, *J. Org. Chem.*, 1986, **51**, 3946.
6. J.C. Amedio and F.D. White, *J. Org. Chem.*, 1986, **54**, 736.
7. S.L. Brown, S.G. Davies, P. Warner, R.H. Jones and K. Prout, *Chem. Comm*, 1985, 1446.
8. S.G. Davies and J.I. Seeman, *Tetrahedron Lett.*, 1984, **25**, 1845.
9. R.L. Hollis and R.C. Ronald, *J. Org. Chem.*, 1981, **46**, 3348.
10. S.G. Davies, I.M. Hedgecock, J.C. Walker, and P. Warner, *Tetrahedron Lett.*, 1984, **25**, 2709.
11. B.T. Golding, R.H. Hall and S. Sakrika, *J.C.S. Perkin I*, 1973, 1214.
12. D.F. Shriver and M.A. Dresdon, "The Manipulation of Air-Sensitive Compounds", Wiley-Interscience, New York, 1986.
13. Oxford Chirality , P.O. Box 412, Oxford, OX1 3QW, U.K.
14. A.C.T. North, D.C. Philips and F.S. Mathews, *Acta Cryst.*, 1986, **A24**, 351.
15. G.M. Sheldrick, "Crystallographic Computing 3", Eds. G.M. Sheldrick, C. Kruger and R. Goddard, Oxford Science Publications, p. 185.