Tetrahedron Vol. 44, No. 6, pp 1637 to 1650, 1988
Printed in Great Britain.

0040-4020/88 $3.00+.00
Pergamon Press plc

Stereochemical Studies on Marine Cyclic Peroxides : An Unequivocal Assignment of Absolute Stereochemistry by Asymmetric Synthesis.

Robert J. Capon and John K. MacLeod
Research School of Chemistry, Australian National University, GPO Box 4,
Canberra, A.C.T. 2601, Australia.

Steven J. Coote, Stephen G. Davies,* G. Lance Gravatt, Isabelle M. Dordor-Hedgecock and Mark Whittaker
The Dyson Perrins Laboratory, South Parks Road, Oxford, OX1 3QY, England.

(*Received in UK* 4 *February* 1988)

Abstract

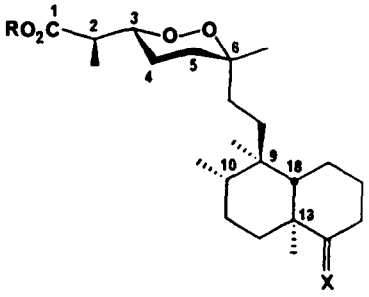
Absolute stereochemical assignments for norterpene cyclic peroxides from marine sponges, previously determined by application of the Horeau procedure of asymmetric esterification, have been independently confirmed by degradation and asymmetric synthesis.

Introduction

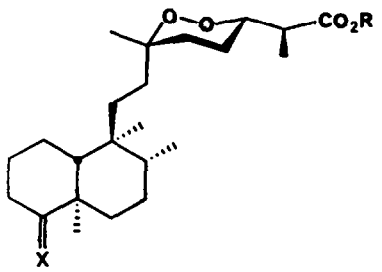
Advances in instrumentation, particularly NMR, have increasingly permitted the assignment of relative stereochemistries to very minor secondary metabolites of varying stability from marine organisms. The assignment of absolute stereochemistries to these compounds has often not been as vigorously pursued, with the result being that they are left unassigned, tentatively proposed from biosynthetic considerations, or assigned by chemical correlation with related compound(s) of known absolute stereochemistry. In the latter case the onus of absolute stereochemical assignment is transferred to that of the "known" compound(s). The cascade effect of such correlations can lead to large numbers of compounds being attributed absolute stereochemistries often based on a single empirical observation, such as the sign of a Cotton effect (CD) or the course of an asymmetric esterification (Horeau procedure).[1] As a consequence it is essential that interpretation of such observations command a high level of confidence.

Recent investigations [2] into a series of marine norterpene cyclic peroxides, exemplified by **1** and **2**, highlighted a contradiction in the assignment of absolute stereochemistry when interpreting both CD and Horeau measurements on these systems. In first reporting the isolation and structure elucidation of sigmosceptrellin A (**1**) [3] and analogues, early workers utilised a CD approach to assigning absolute stereochemistry. Thus a positive CD measurement ($[\theta]_{296}$ +1204) [4] on the derived ketone **3** was interpreted as inferring an **R** configuration about the

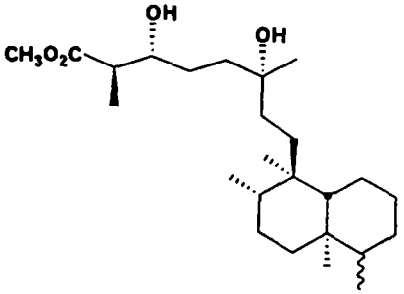
chiral centre adjacent to the carbonyl (C-13).[5] As the relative stereochemistry for **1** had been determined by X-ray analysis,[6] the complete absolute stereochemistry for **1** followed from the assignment about C-13 (opposite to that shown). When examining the structure of *enantio*-sigmosceptrellin A (**2**) we chose to determine its absolute stereochemistry by asymmetric esterification,[2] *i.e.*, the Horeau approach. To this end **2** was methylated and hydrogenated to give the diol **6**, which on esterification with a twofold excess of α-phenyl butyric anhydride returned a preponderance of *laevo* rotatory α-phenyl butyric acid (optical yield 9.3%). This observation was interpreted as implying an S configuration about the secondary hydroxyl (C-3),[5] the same absolute stereochemistry as that attributed to the enantiomeric compound **1** by CD. We have further confirmed this observation by converting **1** to **5** and carrying out a Horeau analysis,[7] and also by degrading **2** to **4** and undertaking a CD measurement. The results were consistent with those observed earlier, with absolute stereochemical assignments made by interpretation of CD measurements conflicting with those based on the Horeau approach. To explain this contradiction it was proposed [2] that, because the CD measurements on 4-keto-5-methyl-*trans*-decalins (*cf.* **3** and **4**) were weak, they were unreliable with respect to assigning absolute stereochemistry.[8] Consequently, Horeau analyses were used as the basis for assigning absolute stereochemistries to a series [2,10,11] of marine norterpene cyclic peroxides. It was recognised, however, that a third unequivocal approach to assigning absolute stereochemistry based on degradation and synthesis would be desirable. In this report we describe such an approach, involving the degradation of *enantio*-sigmosceptrellin A (**2**) to the enantiomerically pure keto diacetate **10**, coupled with the asymmetric synthesis of **10** *via* a stereoselective aldol condensation directed by the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$. [12]



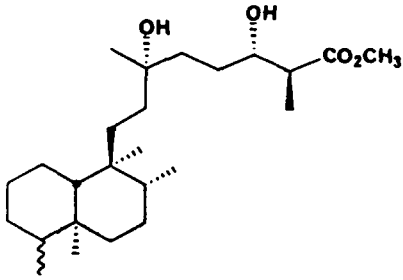
	R	X
1	H	CH_2
3	CH_3	O



	R	X
2	H	CH_2
4	CH_3	O



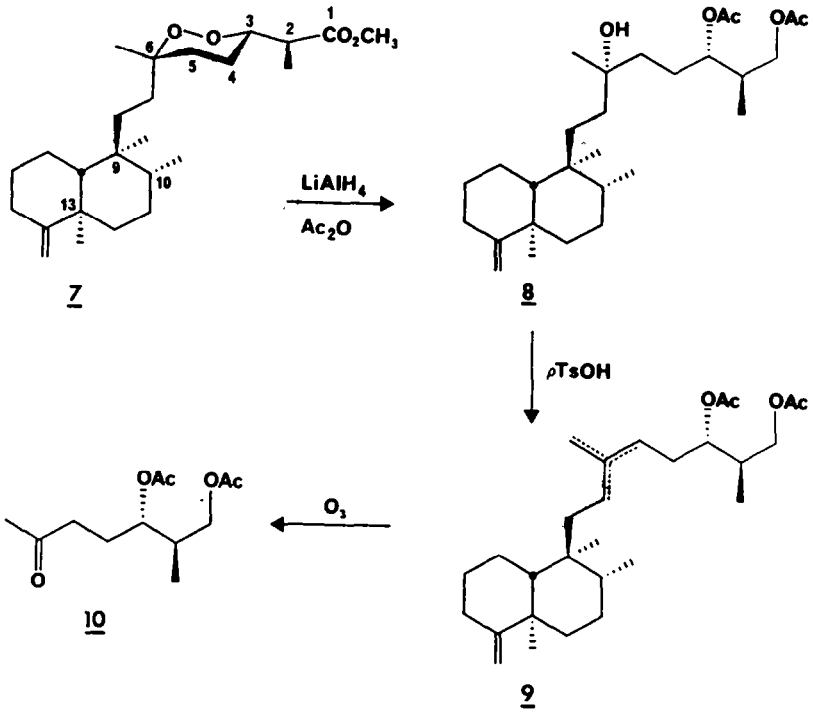
5



6

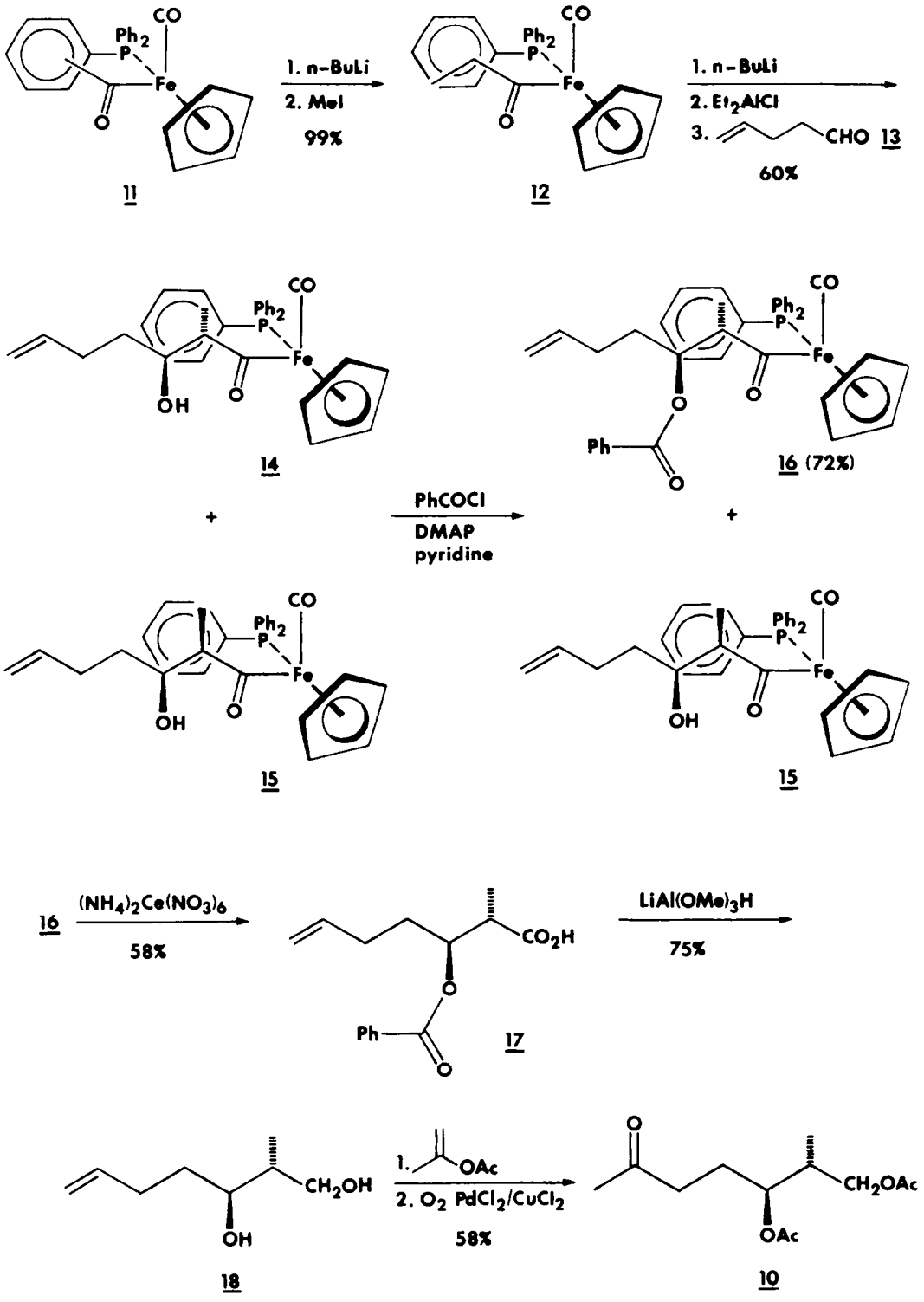
Results and Discussion

Degradation of the methyl ester **7** [13] of *enantio*-sigmosceptrellin A (**2**) was carried out as outlined in Scheme 1. Thus **7** was reduced and acetylated to give the hydroxydiacetate **8**, which on treatment with acid, underwent dehydration to the olefinic mixture **9**. Oxidative cleavage of **9** with ozone yielded as the only isolable product the diacetoxy ketone **10** in which two of the chiral centres from **2** remained intact.



Scheme 1: Degradation of *enantio*-sigmosceptrellin-A

The strategy employed for the unequivocal enantiospecific synthesis of keto diacetate **10** utilised the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$,[14] and was conducted as outlined in Scheme 2. The pivotal step in the synthesis involved an aldol condensation [12] between 4-pentenal **13** [15] and (S)-(+)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)\text{-}COCH_2CH_3]$ (**12**) in order to generate the contiguous chiral centres at C-2 and C-3 of known absolute and relative configurations. Previous work has demonstrated that excellent control over both enantio- and diastereo-selectivities may be achieved in the condensation of simple aldehydes with enolates derived from the iron acyl complex **12**.[12,16] It is possible to obtain the *threo* or the *erythro* product in these reactions in a predictable manner by employing either the derived aluminium or the copper iron acyl enolates respectively.[16] The chosen synthetic route to keto diacetate **10** was initially established starting from the commercially available racemic (S^*)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ (**11**).[17] (S^*)-$[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_2CH_3]$ **12** was prepared from **11** by deprotonation with *n*-butyllithium followed by alkylation with methyl iodide. Treatment of the (S^*)-ethyl acyl complex **12** with *n*-butyllithium and subsequent transmetallation with diethylaluminium chloride generated the corresponding aluminium enolate, which was condensed with 4-pentenal [15] **13** to afford a 15:1 mixture of the diastereoisomeric alcohols (S^*,S^*,S^*)-**14** and (S^*,R^*,S^*)-**15**.



Scheme 2: Asymmetric synthesis of (2R,3S)-2-methyl-6-oxohepta-1,3-diacetate (10)

There are four possible diastereoisomeric products from this aldol reaction, whose relative stereochemistries can be assigned by ^{1}H NMR spectroscopic analysis.[18] The relative configuration of Cα to iron may be determined from the chemical shift of the doublet due to the Cα-methyl group. For S*,S* diastereoisomers it occurs upfield (δ 0.0-0.5 ppm) to that for S*,R* diastereoisomers (δ 0.8-1.3 ppm). This difference in chemical shifts is due to the methyl group for the S*,S* diastereoisomer being held in a conformation such that it is shielded by a proximate phenyl ring of the triphenylphosphine ligand. A conformational analysis for ligands bound to the chiral auxiliary [(η^5-C_5H_5)Fe(CO)(PPh_3)], developed from examination of X-ray crystal structures, molecular graphics and theoretical modelling studies, has recently been reviewed.[19a,b] For all acyl ligands (COR) attached to the chiral auxillary [(η^5-C_5H_5)Fe(CO)(PPh_3)], the most stable conformation is that where the acyl oxygen is *anti* to the carbon monoxide ligand.[19] Conformational control is also exerted over the R group since the 3-dimensional space about the chiral auxiliary [(η^5-C_5H_5)Fe(CO)(PPh_3)] is highly defined. Figure 1 shows a Newman projection along the Cβ to Cα bond for complexes [(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)R] in the *anti* conformation (acyl oxygen with respect to carbon monoxide). Given a requirement to minimise eclipsing interactions, it follows that zone A is the sterically least encumbered space, followed by zone B; whereas, zone C is virtually inaccessible to all but the smallest groups. Thus, the most stable conformation for each of the diastereoisomers will place a hydrogen in zone C. This results in the preferred conformation for the (S*,S*)-diastereoisomer being that where the methyl group is close to the triphenylphosphine ligand. This analysis is consistent with X-ray crystallographic structure determinations reported for (S*,S*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)-COCH(CH_3)CH_2CH_3] [19c] and (S*,R*)-[(η^5-C_5H_5)Re(NO)(PPh_3)CO-CH(CH_3)CH_2Ph].[19d] The configuration of Cβ relative to Cα and iron may be determined by analogy with other aldol reactions, the products of which have been decomplexed to give known *threo* or *erythro* diastereoisomeric α-substituted β-hydroxy carboxylic acids.[12] Thus relative configurations of the two aldol products obtained above were assigned as being (S*,S*,S*)-**14** (methyl doublet at δ 0.39 ppm) and (S*,R*,S*)-**15** (methyl doublet at δ 1.05 ppm).

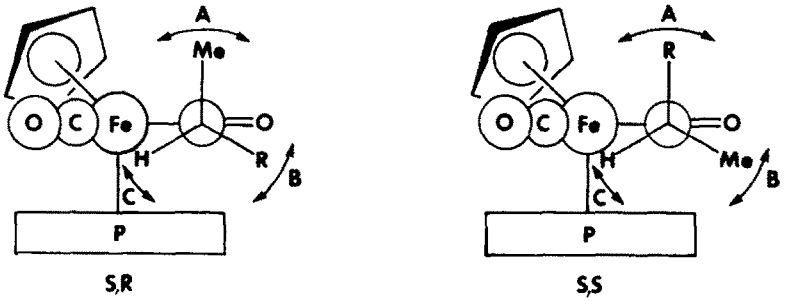


Figure 1: Newman projections along Cβ-Cα for (S,S) and (S,R)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)R]

In order to ensure the optical purity of the target keto diacetate **10**, we considered it necessary to improve the diastereoisomeric purity of **14** at this stage of the synthesis. Whilst it was possible to enhance the ratio of **14**:**15** by repeated flash chromatography, this proved to be an inefficient procedure. However, treatment of the mixture of alcohols **14** and **15** with benzoyl chloride resulted in an efficient kinetic separation to yield the desired (S*,S*,S*)-benzoate **16** as a diastereoisomerically pure product.

This remarkable and novel kinetic separation is due to the chiral auxiliary [(η^5-C_5H_5)Fe(CO)(PPh_3)] imposing a high degree of conformational restraint upon the attached diastereoisomeric acyl ligands of alcohols (S*,S*,S*)-**14** and (S*,R*,S*)-**15**. Following from the conformational analysis described above, the predominant conformation for each diastereoisomer may be predicted on the basis of minimisation of steric interactions (Figure 2). In the predicted conformation for the (S*,S*,S*)-diastereoisomer **14** the hydroxyl moiety is readily accessible for reaction, whereas the hydroxyl group for the (S*,R*,S*)-diastereoisomer **15** is relatively inaccessible since it is restricted to reside in a volume defined by the triphenylphosphine and the plane prescribed by the carbon monoxide and acyl carbon (Figure 2). Hydrogen bonding may occur between the β-hydroxyl and the acyl carbonyl oxygen for the (S*,R*,S*)-diastereoisomer **15**, but not for the (S*,S*,S*)-diastereoisomer **14**. Such hydrogen bonding would serve to reinforce the conformational control of the benzoylation by making the β-hydroxyl in the (S*,R*,S*)-diastereoisomer **15** even less reactive than that for the (S*,S*,S*)-diastereoisomer **14**. However, it should be noted that hydrogen bonding does not occur in the solid state for the α-unsubstituted aldol adduct (S*,S*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH_2CH(OH)Et$],[16b] and hence is unlikely to play a major role in determining the conformational preferences and thereby reactivity of the related α-substituted aldol adduct **15**.

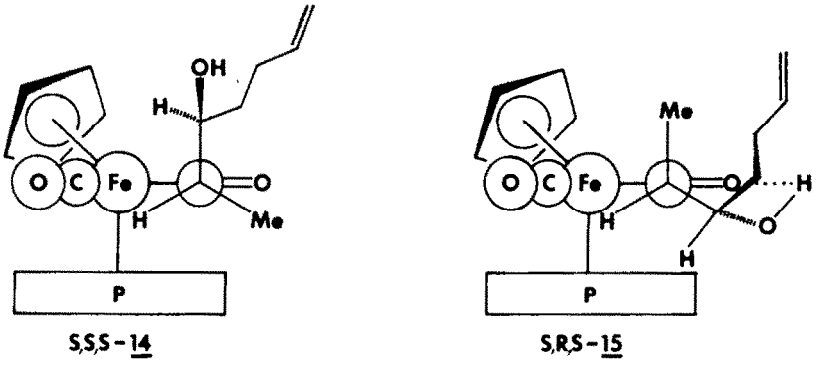


Figure 2: Newman projections along Cβ-Cα for (S,S,S) and (S,R,S)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)CH(OH)CH_2CH_2CH{=}CH_2$] (**14**) and (**15**)

Figure 3 shows the molecular structure of racemic (S*,S*,S*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)$COCH(CH_3)$-$CH(OCOPh)CH_2CH_2CH{=}CH_2$] (**16**) as determined by an X-ray crystallographic analysis of a single crystal. Final atomic co-ordinates are listed in Table 1. In common with other acyl complexes of [(η^5-C_5H_5)Fe-(CO)(PPh_3)], the geometry about iron is close to octahedral, and the acyl oxygen is *anti* to the carbon monoxide ligand. This is the first structural determination of an α-substituted β-hydroxyl iron acetyl complex and not only confirms that the conformation adopted in the solid state is as predicted above, but also that the relative stereochemistry is (S*,S*,S*) as predicted from ^{1}H NMR analysis of the aldol adduct **14**. This in turn confirms the assignments of relative configurations for the aldol adducts which we reported in our earlier model studies.[12] Decomplexation of (S*,S*,S*)-benzoate **16** with cerium(IV) afforded (2S*,3S*)-benzoyloxy acid **17**. ^{1}H NMR (300 MHz) analysis confirmed that this material was diastereoisomerically pure (>200:1). Reduction of benzoyloxy acid **17** to the corresponding (2S*,3R*)-diol **18** was accomplished using trimethoxylithium aluminium hydride[20] as the reagent of choice. ^{1}H NMR analysis of diol **18** revealed that a small amount (<1%) of epimerisation at C-2 had occured during the reduction. Attempts to accomplish the above reduction using a range

of other reducing agents [including lithium aluminium hydride, sodium bis(2-methoxyethoxy)aluminium hydride and monomethoxylithium aluminium hydride] afforded inseparable mixtures of the diol **18** along with over-reduced, fully saturated material. Elaboration of diol **18** to the target (2S*,3R*)-keto diacetate **10** was acheived by sequential diacetylation and palladium catalysed oxidation [21] of the the terminal olefinic moiety to the corresponding methyl ketone. The infra-red, ^1H NMR, ^{13}C NMR, and mass spectroscopic data obtained for the synthetic keto diacetate **10** were identical in all respects to those of the compound derived from natural material.

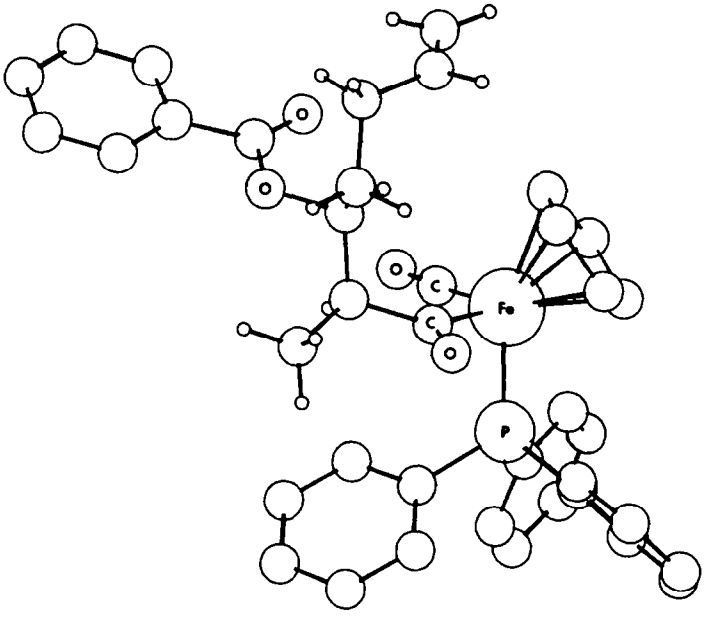


Figure 3: Molecular structure of
(S^*,S^*,S^*)-[$(\eta^5$-$C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(OCOPh)CH_2CH_2CH{=}CH_2$] (**16**)

The above results have confirmed the viability of the strategy outlined in Scheme 2, and allowed an unambiguous assignment of the relative stereochemistry in keto diacetate **10**. The above synthetic route was therefore repeated employing commercially available, enantiomerically pure, (S)-(+)-iron acetyl **11** to afford (2R,3S)-keto diacetate **10** as a colourless oil in 11% overall yield.

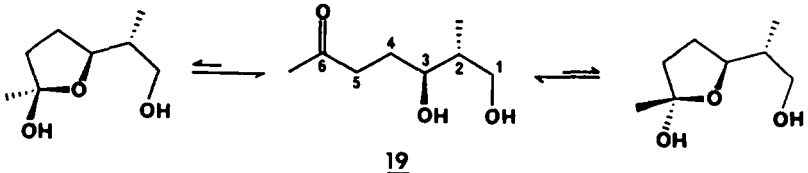
Measurements of the $[\alpha]_D$ values for synthetic and naturally derived **10** in chloroform gave small and unexpectedly opposite rotations (synthetic -1.3 (*c* 3.0); natural +2.4 (*c* 1.0)), while in ethanol both values were larger and negative (synthetic -7.0 (*c* 1.6); natural -4.0 (*c* 0.6)). The CD spectra of both compounds were identical ($[\theta]_{275}$ +400; $[\theta]_{215}$ -1200). These latter results, while confirming that synthetic and natural **10** had the same 2R,3S absolute configuration, nevertheless suggested the presence of a small amount of an impurity with a high and positive $[\alpha]_D$ value in the degradation product. This could not be detected by NMR spectroscopy or separated from **10** by HPLC or GC. Further transformation of **10** to the acetal **20** was, therefore, carried out to try

Table 1: Final atomic co-ordinates for

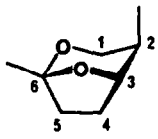
(S^*,S^*,S^*)-[$(\eta^5$-$C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(OCOPh)CH_2CH_2CH{=}CH_2$] (16)

Atom	x/a	y/b	z/c	U(iso)
FE(1)	5025.9(3)	-1673.2(9)	6667.3(4)	474
P(1)	4649.2(5)	-431(2)	7574.6(6)	476
C(1)	5172(3)	156(7)	6227(3)	623
C(2)	5819(2)	-1838(6)	7163(2)	480
C(3)	6383(2)	-809(6)	6956(2)	503
C(4)	6846(3)	-568(8)	7561(3)	707
C(5)	6669(2)	-1544(6)	6315(3)	511
C(6)	7021(3)	-3126(7)	6441(3)	723
C(7)	7223(4)	-3973(10)	5774(5)	944
C(8)	6685(7)	-4721(19)	5397(7)	1363
C(9)	6457(8)	-4150(21)	4838(9)	1734
C(10)	7047(2)	282(6)	5435(2)	533
C(11)	7576(2)	1374(6)	5269(3)	519
C(12)	7573(3)	2094(7)	4612(3)	710
C(13)	8061(4)	3072(9)	4425(4)	812
C(14)	8534(4)	3322(9)	4881(4)	870
C(15)	8541(3)	2655(8)	5544(4)	778
C(16)	8058(2)	1665(7)	5730(3)	616
C(17)	4732(3)	-4115(7)	6790(3)	677
C(18)	5196(3)	-4036(7)	6288(3)	676
C(19)	4994(3)	-3053(8)	5734(3)	682
C(20)	4392(3)	-2510(8)	5880(3)	672
C(21)	4234(3)	-3170(7)	6532(3)	671
C(22)	4016(2)	997(7)	7390(3)	584
C(23)	3903(3)	2345(7)	7811(3)	639
C(24)	3416(3)	3371(8)	7680(4)	776
C(25)	3026(4)	3062(11)	7127(4)	995
C(26)	3128(5)	1764(15)	6694(5)	1182
C(27)	3623(4)	756(11)	6821(4)	904
C(28)	5168(2)	866(6)	8094(3)	503
C(29)	5460(3)	2155(7)	7764(3)	660
C(30)	5848(3)	3200(8)	8126(4)	781
C(31)	5953(4)	2985(8)	8829(4)	842
C(32)	5658(4)	1751(8)	9174(4)	832
C(33)	5269(3)	701(7)	8807(3)	628
C(34)	4325(2)	-1784(6)	8237(2)	505
C(35)	3738(2)	-1633(7)	8477(3)	660
C(36)	3514(3)	-2669(10)	8981(3)	770
C(37)	3873(3)	-3927(9)	9235(3)	727
C(38)	4457(3)	-4121(7)	8998(3)	663
C(39)	4688(3)	-3053(7)	8498(3)	607
O(1)	5245	1312	5903	803
O(2)	5919	-2811	7639	588
O(3)	7127	-384	6065	556
O(4)	6608	74	5064	773

to remove the impurity. Treatment of **10** with methanolic ammonia yielded the equilibrium mixture **19** (in $CHCl_3$ the equilibrium ratio was hemiacetal:diol:hemiacetal, 1:2:1). Both synthetic and naturally derived **19** showed similar optical properties (synthetic $[\alpha]_D$ -9.0 (*c* 0.65, $CHCl_3$); natural $[\alpha]_D$ -10.0 (*c* 0.28, $CHCl_3$)). Treatment of **19** with a trace of trifluoroacetic acid resulted in rapid and quantitative stereoselective cyclisation to the acetal **20**. Not only did cyclisation of **19** to **20** involve the generation of a third chiral centre (C-6), but the resulting conformational rigidity permitted an assessment [22] of the stereochemical purity about C-2. Thus it was shown that both synthetic and naturally derived acetal **20** were essentially diastereoisomerically pure (both contained traces, <1% and <2% respectively, of the C-2 epimer) and, furthermore, that both possessed the same 2R,3S absolute stereochemistry (synthetic **20** $[\alpha]_D$ +3.0 (*c* 0.30, $CHCl_3$); natural **20** $[\alpha]_D$ +3.0 (*c* 0.32, $CHCl_3$)).



19



20

From the above , it is possible to conclude that previous application of the Horeau procedure to suitable derivatives of marine norterpene cyclic peroxides [2,10,11] did result in correct absolute stereochemical assignments. Furthermore, this result serves to highlight the need to exercise caution when using small CD measurements to assign absolute stereochemistries.

Experimental

All reactions and purifications were performed under nitrogen atmosphere using standard vacuum line and Schlenk tube techniques.[23] Removal of all solvents was carried out under reduced pressure. THF was dried over sodium benzophenone ketyl and distilled. Dichloromethane was distilled from calcium hydride, and hexane refers to that fraction boiling in the range 67-70°C. Neat diethylaluminium chloride as supplied by Schering, was freshly prepared as a 2.0 M solution in toluene, and *n*-butyllithium (2.5 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 either a Bruker WH 300 spectrometer at 300.13 MHz, a Jeol JNM-FX-200 spectrometer at 200 MHz or a Varian XL-200-E spectrometer at 200 MHz and referenced to residual protio-solvent, with chemical shifts being reported as δ ppm from $(CH_3)_4Si$. Carbon-13 n.m.r. spectra were recorded on either a Bruker AM 250 spectrometer at 62.90 MHz, a Jeol JNM-FX-200 spectrometer at 50 MHz or a Varian XL-200-E spectrometer at 50 MHz using $CDCl_3$ as 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 either a V.G. micromass ZAB 2F instrument, a V.G. micromass 7070F instrument or a V.G. Masslab 20-250 instrument using EI and field desorption (FD) techniques. Chemical ionisation mass spectra were recorded on a V.G. micromass

7070F instrument using ammonia as the reagent gas. High resolution accurate mass measurements were determined on either an MS 902(EI) or 7070F(CI). Optical rotations were recorded on either a Perkin-Elmer 241 polarimeter or a Perkin-Elmer 121 polarimeter, and CD spectra on a Cary 61 spectropolarimeter. Elemental analyses were performed by the Dyson Perrins Laboratory Analytical Service (Oxford, U.K.).

The synthetic sequence was initially conducted starting from racemic (S*)-[(η^5-C_5H_5)Fe(CO)-(PPh3)COCH3],[17] however for the sake of brevity only the synthetic sequence starting from (S)-(+)-[(η^5-C_5H_5)-Fe(CO)(PPh3)COCH3] [17] is reported below.

Degradation of cyclic peroxide **7**. - To a solution of the cyclic peroxide **7** (100 mg) in dry ether (5 ml) was added excess $LiAlH_4$ (40 mg) and the resulting mixture stirred under reflux for 2 h. The reaction was quenched by the addition of 10% aqueous HCl (4ml) and extracted with EtOAc. Acetylation of the crude reaction product with acetic anhydride and pyridine at room temperature yielded the hydroxy diacetate **8** (95 mg, 83%) as a stable colourless oil; $[\alpha]_D$ +25 (*c* 0.64, $CHCl_3$); ^{1}H n.m.r. (200 MHz) δ 4.90 (1H, bm, 3-H), 4.50 (2H, bs, 18-H_2), 4.01 (2H, d ABq, J 6.4 Hz, 10.0 Hz, 1-H_2), 2.06 (3H, s) and 2.05 (3H, s, 2xOCOCH3), 1.13 (3H, s, 6-CH_3), 1.04 (3H, s, 13-CH_3), 0.97 (3H, d, J 7.0 Hz, 2-CH_3), 0.79 (3H, d, J 6.0 Hz, 10-CH_3), 0.74 (3H, s, 9-CH_3); EIMS 446 (M^+-H_2O, 4%), 404 (M^+-HOAc, 1), 386 (3), 371 (5), 245 (18), 191 (47), 185 (42), 78 (100); CIMS (NH_3) 482 ([$M+NH_4$]$^+$, 4%), 464 (9), 447 (100), 387 (31), 245 (4), 191 (14); HRMS 446.3394 (M^+-H_2O requires $C_{28}H_{46}O_4$ 446.3396).

Dehydration of hydroxy diacetate **8**. - A mixture of the hydroxy diacetate **8** (90 mg) and p-TsOH (10 mg) in benzene (5 ml) was stirred under reflux for 2 h, after which the reaction mixture was filtered and evaporated to dryness. Purification by HPLC (elution with 10% EtOAc/hexane through a 10cm x 0.8 cm 10μ radial pak silica column) yielded **9** (79 mg, 91%) as a mixture of dehydration products which were not separated but ozonolysed without further characterisation; EIMS 446 (M^+, 0.5%), 191 (100); HRMS 446.3407 (M^+ requires $C_{28}H_{46}O_4$ 446.3396).

Ozonolysis of **9**. - A sample of **9** (79 mg) in EtOAc (5 ml) at -78°C was treated with a stream of ozonolised oxygen for 10 min. after which Jones reagent (0.5 ml) was added and the mixture allowed to warm to room temperature. Extraction with EtOAc yielded a complex mixture of products which were methylated with ethereal diazomethane prior to purification. HPLC (elution with 40% EtOAc/hexane through a 10 cm x 0.8 cm 10μ radial pak silica column) of the material yielded the diacetoxy ketone **10** (13 mg, 30%) as a stable colourless oil; $[\alpha]_D$ +2.4 (*c* 1.0, CHCl3); $[\alpha]_D$ -4.0 (*c* 0.6, EtOH); CD $[\theta]_{275}$ +400, $[\theta]_{215}$ -1200 (*c* 0.3, EtOH); ^{1}H (200 MHz) n.m.r. δ 4.88 (1H, ddd, J 9.7 Hz, 6.4 Hz, 3.4 Hz, 3-H), 4.01 (2H, d, J 6.4 Hz, 1-H_2), 2.15 (3H, s, 6-CH_3), 2.06 (6H, s, 2x OCOCH3), 0.98 (3H, d, J 7.0 Hz, 2-CH3); ^{13}C n.m.r. (50 MHz) δ 207.5 (s, 6-C), 171.0 (s, O<u>C</u>OCH3), 170.5 (s, O<u>C</u>OCH3), 74.2 (d, 3-C), 65.5 (t, 1-C), 39.4 (t, 5-C), 36.4 (d, 2-C), 29.9 (q, 6-CH3), 25.2 (t, 4-C), 20.9 (q, OCO<u>C</u>H3), 20.8 (q, OCO<u>C</u>H3), 13.5 (q, 2-CH3); EIMS 201 (M^+-CH_3CO, <1%), 187 (M^+-C_3H_5O, 20), 145 (50), 101 (100); CIMS (NH_3) 262 ([$M+NH_4$]$^+$, 100%); HRMS 187.0966 (M^+-C_3H_5O requires $C_9H_{15}O_4$ 187.0970).

Preparation of (S)-[(η^5-C_5H_5)Fe(CO)(PPh3)COCH2CH3] **(12)**. - *n*-Butyllithium (7.1 ml, 17.75 mmol) was added to an orange solution of (S)-[(η^5-C_5H_5)Fe(CO)(PPh3)COCH3] **(11)** [17] (4.0 g, 8.81 mmol) in THF (80 ml) at -78°C and the resulting dark red solution was stirred for 1 h. Methyl iodide (4.0 ml, 35.2 mmol) was then added to the reaction mixture which was stirred at -78°C for a further 4 h. The resulting solution was quenched with methanol and allowed to warm slowly to ambient temperature, before being concentrated and filtered through alumina (Grade V). The crude product was chromatographed on alumina (Grade I) to give an orange band (dichloromethane:ethyl acetate, 4:1 elution) of (S)-[(η^5-C_5H_5)Fe(CO)(PPh3)COCH2CH3] **(12)** (4.1 g, 99%), $[\alpha]_{546}^{20}$ +271 (c 2.0, C_6H_6). The spectroscopic data obtained for this material was identical in all respects with that obtained for racemic (S*)-[(η^5-C_5H_5)-Fe(CO)(PPh3)COCH2CH3]. [24]

Preparation of (S,S,S)-[(η^5-C_5H_5)Fe(CO)(PPh3)COCH(CH3)CH(OH)CH2CH2CH=CH2] **(14)**. - *n*-Butyllithium (2.8 ml, 6.86 mmol) was added to an orange solution of (S)-[(η^5-C_5H_5)Fe(CO)(PPh3)COCH2CH3] **(12)** (2.141 g, 4.57 mmol) in THF (80 ml) at -78°C and the resulting dark-purple mixture was stirred at -78°C for 30 min. Diethylaluminium chloride (11.5 ml, 22.85 mmol) was added to the reaction mixture, which was warmed to -40°C and stirred for 2 h. The mixture was cooled to -100°C and a solution of 4-pentenal **13** [15] (1.85 g, 22.02

mmol) in THF (10 ml) was added dropwise (5 min.). After stirring at -100°C for 2.5 h, methanol (5 ml) was added followed by solid $NaHCO_3$ (1.5 g) and the mixture allowed to warm slowly to ambient. The solvent was removed, water (100 ml) added to the residue and the mixture extracted with dichloromethane (3x40 ml). Concentration and chromatography over alumina (Grade I) (dichloromethane elution) gave a red band of rearranged material,[25] followed by an orange band (dichloromethane:ethyl acetate, 1:1 elution) of a 15:1 mixture of (S,S,S)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH_3)CH(OH)$CH_2CH_2CH{=}CH_2$] (**14**) and (S,R,S)-[(η^5-C_5H_5)Fe(CO)(PPh3)COCH(CH_3)CH(OH)$CH_2CH_2CH{=}CH_2$] (**15**) (1.151 g, 60%). Repeated chromatography (x3) (flash grade silica gel, ether:40/60 petrol 3:1 elution) followed by crystallisation from dichloromethane/hexane solution afforded the desired (S,S,S)-diastereoisomer **14** (30:1 d.e. as determined by ^{31}P n.m.r.), (Found C 69.5; H 6.1; P 5.6. $C_{32}H_{33}FeO_3P$ requires C 69.6; H 6.0; P 5.6%); $[\alpha]_D^{20}$ +195, $[\alpha]_{578}^{20}$ +219, $[\alpha]_{546}^{20}$ +352 (*c* 0.06, C_6H_6); $\nu_{max.}$ 3360w (O-H), 3040s (C-H), 2980m (C-H), 1910vs (C=O), 1590s cm^{-1} (C=O); ^{1}H n.m.r. (300 MHz) δ 7.62-7.32 (15H, m, Ph), 5.82 (1H, ddt, J_{trans} 17.0 Hz, J_{cis} 10.2 Hz, $J_{1,2}$ 6.7 Hz, C<u>H</u>=CH_2), 5.08-4.93 (2H, m, CH=C<u>H</u>$_2$), 4.44 (5H, d, J_{PH} 1.3 Hz, C_5H_5), 3.62 (1H, m, C<u>H</u>OH), 2.44 (1H, d, $J_{1,2}$ 6.7, 4.9 Hz, OH), 2.35-2.02 (2H, m, C<u>H</u>$_2$CH$_2$CH=), 1.41 (2H, m, CH$_2$C<u>H</u>$_2$CH=), 0.39 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3); ^{13}C{^{1}H} (62.90 MHz) n.m.r. δ 284.95 (d, $^2J_{PC}$ 20.4 Hz, C=O), 220.98 (d, $^2J_{PC}$ 31.2 Hz, C=O), 138.78 (s, <u>C</u>H=CH_2), 136.59 (d, $^1J_{PC}$ 42.6 Hz, Ph C_{ipso}), 133.53 (d, $^2J_{PC}$ 9.7 Hz, Ph C_{ortho}), 129.63 (s, Ph C_{para}), 127.92 (d, $^3J_{PC}$ 9.3 Hz, Ph C_{meta}), 114.52 (s, CH=<u>C</u>H$_2$), 85.35 (s, C_5H_5), 73.03 (s, CH), 72.92 (s, CH), 33.23 (s, CH_2) 30.30 (s, CH_2), 11.81 (s, CH_3); ^{31}P{^{1}H} n.m.r. δ 71.46; FDEIMS 552 (M^+).

Preparation of (S,S,S)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH_3)CH(OCOPh)$CH_2CH_2CH{=}CH_2$] (**16**). - Benzoyl chloride (0.41 ml, 3.54 mmol), followed by 4-dimethylamino pyridine (0.29 g, 2.38 mmol) was added to an orange solution of a 15:1 mixture of (S,S,S)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH_3)CH(OH)$CH_2CH_2CH{=}CH_2$] (**14**) and (S,R,S)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH_3)CH(OH)$CH_2CH_2CH{=}CH_2$] (**15**) (1.30 g, 2.36 mmol) in pyridine (20 ml) at ambient temperature and the resulting mixture was stirred at ambient temperature for 20 h. Concentration and chromatography over flash silica afforded an orange band (dichloromethane elution) of (S,S,S)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH_3)CH(OCOPh)$CH_2CH_2CH{=}CH_2$] (**16**) (1.12 g, 72%) (>42:1 d.e. as determined by ^{31}P n.m.r.), (Found C 71.5; H 5.8; P 4.8. $C_{39}H_{37}FeO_4P$ requires C 71.4; H 5.7; P 4.7%); $[\alpha]_D^{20}$ +193, $[\alpha]_{578}^{20}$ +218, $[\alpha]_{546}^{20}$ +328 (*c* 0.05, C_6H_6); $\nu_{max.}$ 3040s (C-H), 2980m (C-H), 1910vs (C=O), 1705s (C=O), 1600s cm^{-1} (C=O); ^{1}H n.m.r. (300 MHz) δ 8.10-8.06 (2H, m, Ph), 7.65-7.32 (18H, m, Ph), 5.88-5.74 (2H, m, C<u>H</u>=CH_2 and C<u>H</u>OCOPh), 5.03-4.93 (2H, m, CH=C<u>H</u>$_2$), 4.47 (5H, d, J_{PH} 1.1 Hz, C_5H_5), 3.50 (1H, dq, $J_{2,3}$ 6.8Hz, $J_{1,2}$ 6.8Hz, C<u>H</u>CH_3), 2.13-2.02 (2H, m, C<u>H</u>$_2$CH$_2$CH=), 1.67-1.50 (2H, m, CH$_2$C<u>H</u>$_2$CH=), 0.29 (3H, d, $J_{1,2}$ 6.8 Hz, CH_3); ^{13}C{^{1}H} n.m.r. (62.90 MHz) δ 278.54 (d, $^2J_{PC}$ 24.0 Hz, C=O), 220.37 (d, $^2J_{PC}$ 31.6 Hz, C=O), 165.80 (s, Ph<u>C</u>O) 137.99 (s, <u>C</u>H=CH_2), 136.53 (d, $^1J_{PC}$ 42.7 Hz, Ph C_{ipso}), 133.53 (d, $^2J_{PC}$ 9.4 Hz, Ph C_{ortho}), 132.58 (s, PhCO C_{ortho}), 130.99 (s, PhCO C_{ipso}), 129.69 (s) and 129.61 (s, Ph C_{para} and PhCO C_{para}), 128.18 (d, $^3J_{PC}$ 9.3 Hz, Ph C_{meta}), 127.95 (s, PhCO C_{meta}), 115.00 (s, CH=<u>C</u>H$_2$), 85.35 (s, C_5H_5), 73.00 (s, C<u>H</u>OCOPh), 70.66 (d, $^3J_{PC}$ 5.5Hz, C<u>H</u>CH_3), 30.10 (s, CH_2) 28.79 (s, CH_2), 9.86 (s, CH_3); ^{31}P{^{1}H} n.m.r. δ 70.68; FDEIMS 656 (M^+).

Preparation of (2S,3S)-2-methyl-3-benzoyloxy-6-hepten-1-oic acid (**17**). - Ceric ammonium nitrate (3.80 g, 6.93 mmol) was added to a stirred orange solution of (S,S,S)-[(η^5-C_5H_5)Fe(CO)(PPh$_3$)COCH(CH_3)CH(OCOPh)-$CH_2CH_2CH{=}CH_2$] (**16**) (0.90g, 1.37 mmol) in 5% aqueous THF (50ml) at -40°C. The resulting dark brown solution was allowed to warm slowly to ambient temperature and stirred for 3.5 h. The solvent was removed *in vacuo* (0°C), 5% aqueous sodium hydroxide solution (100 ml) added to the residue and the mixture extracted with ether (200 ml). The separated aqueous phase was re-acidified with conc. hydrochloric acid and extracted with ether (2x200 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* (0°C) to give a brown oil, which was purified by p.t.l.c. (dichloromethane:ether, 4:1 elution) to afford (2S,3S)-2-methyl-3-benzoyloxy-6-hepten-1-oic acid (**17**) (0.1976 g, 58%); $[\alpha]_D^{27}$ +6.0 (*c* 0.8, $CHCl_3$); $\nu_{max.}$ 3400m (O-H), 3100m (O-H), 2900m (C-H), 1710s cm^{-1} (C=O); ^{1}H n.m.r. (300 MHz) δ 8.13-8.04 (2H, m, Ph), 7.65-7.51 (1H, m, Ph), 7.48-7.42 (2H, m, Ph), 5.82 (1H, ddt, J_{trans} 17.0 Hz, J_{cis} 10.3 Hz, $J_{5,6}$ 6.7 Hz, C<u>H</u>=CH_2), 5.43 (1H, dt, $J_{2,3}$ 6.9Hz, $J_{3,4}$ 5.8Hz, C<u>H</u>OCOPh), 5.08-4.96 (2H, m, CH=C<u>H</u>$_2$), 3.01 (1H, dq, $J_{2,3}$ 6.0Hz, $J_{2,Me}$ 7.1Hz, C<u>H</u>CH_3), 2.18 (2H, broadq, J 7.3Hz,CH_2C<u>H</u>$_2$CHOCOPh), 1.92-1.84 (2H, m, C<u>H</u>$_2$CH$_2$CHOCOPh), 1.28 (3H, d, $J_{2,Me}$ 7.1Hz, CHC<u>H</u>$_3$); ^{13}C n.m.r. (62.90 MHz) δ 178.29 (s, CO_2H), 171.27 (s, O<u>C</u>OPh), 132.99 (d, Ph C_{para}), 130.19 (s, Ph C_{ipso}), 129.69 (d) and 128.46 (d, Ph C_{meta} and C_{ortho}), 115.23 (t, CH=<u>C</u>H$_2$), 74.45 (d, <u>C</u>HOCOPh), 42.98 (d, <u>C</u>HCH$_3$), 30.48 (t) and 29.48 (t, <u>C</u>H$_2$<u>C</u>H$_2$CH=CH_2), 12.54 (q, CH_3); CIMS (NH_3) 280 ($M+NH_4$)$^+$, 263 $(M+H)^+$, 245 (MH^+-H_2O), 105 ($PhCO^+$).

A microanalyically pure sample was not obtained since this material underwent rapid hydrolysis. The material was reduced without any further purification.

Preparation of (2R,3S)-2-methyl-6-hepten-1,3-diol (**18**). - A solution of freshly prepared trimethoxylithium aluminium hydride (3.0 ml of a 1.0 M solution in THF) was added to a stirred solution of (2S,3S)-2-methyl-3-benzoyloxy-6-hepten-1-oic acid (**17**) (0.14 g, 0.53 mmol) in THF (30 ml) at 0-5°C. The resulting colourless solution was allowed to slowly warm to ambient temperature and stirred for 15 h. The reaction mixture was then diluted with 5% aqueous hydrochloric acid (20 ml) and extracted with dichloromethane (3x30 ml). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo* (0°C) to give a near colourless oil. The crude product was purified by p.t.l.c. (ether elution) to afford (2R,3S)-2-methyl-6-hepten-1,3-diol (**18**) (0.057 g, 75%), (Found C 66.2; H 11.3. $C_8H_{16}O_2$ requires C 66.6; H 11.2%); $[\alpha]_D^{25.5}$ -29.4 (*c* 0.74, $CHCl_3$); $\nu_{max.}$ 3600s (OH), 3500s (O-H), 2890m (C-H), 1670w (CH=CH_2), 1020s cm^{-1} (C-O); ^1H n.m.r. (300 MHz) δ 5.87 (1H, ddt, J_{trans} 17.0 Hz, J_{cis} 10.3 Hz, $J_{5,6}$ 6.7 Hz, C<u>H</u>=CH_2), 5.12-4.98 (2H, m, CH=C<u>H</u>$_2$), 3.64 (2H, dd, J_{gem} 10.8Hz, $J_{1,2}$ 7.2Hz, C<u>H</u>$_2$OH), 3.60 (1H, dt, $J_{2,3}$ 3.2Hz, $J_{3,4}$ 8.3Hz, C<u>H</u>OH), 2.56 (2H, broad s, O<u>H</u>), 2.28 (2H, m, CH_2C<u>H</u>$_2$CHOH), 1.78-1.54 (3H, m, C<u>H</u>$_2$$CH_2$CHOH and C<u>H</u>$CH_3$), 0.91 (3H, d, $J_{2,Me}$ 7.0Hz, CHC<u>H</u>$_3$); ^{13}C n.m.r. (62.90 MHz) δ 138.57 (d, <u>C</u>H=CH_2), 114.99 (t, CH=<u>C</u>H$_2$), 76.86 (d, <u>C</u>HOH), 67.62 (t, <u>C</u>H$_2$OH), 39.95 (d <u>C</u>HCH$_3$), 34.43 (t) and 29.74 (t, <u>C</u>H$_2$<u>C</u>H$_2$CH=CH_2), 13.87 (q, <u>C</u>H$_3$); CIMS (NH_3) 162 $(M+NH_4)^+$, 145 $(M+H)^+$, 127 (MH^+-H_2O), 109 (MH^+-H_2O-H_2O).

Preparation of (2R,3S)-2-methyl-6-oxohepta-1,3-diacetate (**10**). - A stirred mixture of (2R,3S)-2-methyl-6-hepten-1,3-diol (**18**) (52.1 mg, 0.36 mmol), isopropenyl acetate (3.5 ml) and p-toluene sulphonic acid (5 mg) was heated in an oil bath at 100°C for 18 h (by-product acetone was removed by distillation). The mixture was cooled and excess isopropenyl acetate removed. The residue was disssolved in dichloromethane and filtered through a short pad of flash silica. The solvent was removed to give (2R,3S)-2-methyl-6-heptenyl-1,3-diacetate as a crude oil which was oxidised without further purification.

A mixture of palladium(II) chloride (22.9 mg, 0.13 mmol) and copper(I) chloride (102.8 mg, 1.04 mmol) in DMF (1 ml) and water (0.07 ml) was stirred for 1 h under oxygen; a slow colour change from black to green occurred. A solution of the crude (2R,3S)-2-methyl-6-heptenyl-1,3-diacetate (as prepared above) in DMF (1 ml) was added and the mixture stirred for 18 h at ambient under oxygen. 1N Hydrochloric acid (10 ml) was added and the mixture extracted with diethyl ether (5x25 ml). The organic extracts were washed with saturated $NaHCO_3$ (10 ml), water (10 ml), brine (10 ml), and dried over Na_2SO_4. Removal of solvent gave a straw coloured oil, which was purified by p.t.l.c. to give (2R,3S)-2-methyl-6-oxohepta-1,3-diacetate (**10**) (50.9 mg, 58%); $[\alpha]_D^{24}$ -1.3 (*c* 3.0, $CHCl_3$); -7.0 (*c* 1.6, EtOH); CD $[\theta]_{275}$ +400, $[\theta]_{215}$ -1200 (*c* 0.12, EtOH); $\nu_{max.}$ 2960m (C-H), 1725vs (C=O), 1715s (C=O) 1250vs cm^{-1} (C-C(=O)-O); ^1H n.m.r. (300 MHz) δ 4.86 (1H, ddd, $J_{1,2}$ 9.5, 6.4, 3.2 Hz, C<u>H</u>OAc), 3.99 (1H, d, $J_{1,2}$ 5.6 Hz, C<u>H</u>HOAc), 3.98 (1H, d, $J_{1,2}$ 6.1 Hz,CH<u>H</u>OAc), 2.45 (2H, m, C(=O)CH_2), 2.18-1.68 (3H, m, C(=O)CH_2C<u>H</u>$_2$ and CHC<u>H</u>$_3$), 2.13 (3H, s, C(=O)CH_3), 2.04 (6H, s, 2 C(=O)CH_3), 0.97 (3H, d, $J_{1,2}$ 7.0 Hz, CH_3); ^{13}C n.m.r. (62.90 MHz) δ 207.48 (s, 6-C), 170.99 (s, CH_3<u>C</u>=O), 170.66 (s, CH_3<u>C</u>=O), 74.21 (d, 3-C), 65.50 (t, 1-C), 39.43 (t, 5-C), 36.36 (d, 2-C), 29.92 (q, 7-C), 25.24 (t, 4-C), 20.93 (q, <u>C</u>H$_3$C=O), 20.83 (q, <u>C</u>H$_3$C=O), 13.45 (q, CH_3); CIMS (NH_3) 262 $(M+NH_4)^+$, 245 $(M+H)^+$, 185 (MH^+-CH_3COOH).

Hydrolysis of **10** *from degradation of* **7**. - Treatment of the diacetoxy ketone **10** (6 mg) in methanol (1 ml) with NH_4OH (0.2 ml) at room temperature for 1h followed by evaporation under reduced pressure resulted in a quantitative recovery of the equilibrium mixture **19**; $[\alpha]_D$ -10.0 (*c* 0.28, $CHCl_3$); ^1H n.m.r. (200 MHz) resolved hemiacetal resonances δ 4.04 (dt, J 9.0 Hz, 7.0 Hz, 3-H), 3.88 (dt, J 6.2 Hz, 8.8 Hz, 3-H), 1.54 (s) and 1.53 (s, 2x 6-CH_3), 0.84 (d, J 7.2 Hz) and 0.82 (d, J 7.2 Hz, 2x 2-CH_3); resolved keto diol resonances δ 3.77 (dd, J 3.8 Hz, 10.6 Hz, 1-H_a), 3.53 (dt, J 3.2 Hz, 8.4 Hz, 3-H), 2.66 (t, J 6.8 Hz, 5-H_2), 2.19 (s, 6-CH_3), 0.87 (d, J 6.9 Hz, 2-CH_3); unresolved resonances δ 3.7-3.6 (bm, 1-H_2), 2.1-1.6 (bm, 2-H, 4-H_2 and 5-H_2); EIMS 143 (M^+-OH, 8%), 125 , 101, 83, 71, 55, 43 (100); CIMS (NH_3) 143 ($[M-H_2O+H]^+$, 100%), 125 (39).

Hydrolysis of synthetic **10**. - Treatment of compound **10** (12 mg), derived synthetically, under the same conditions as above gave the same equilibrium mixture **19** $[\alpha]_D$ -9.0 (*c* 0.65, $CHCl_3$) with identical ^1H n.m.r. and EI/CI mass spectra.

Cyclisation of naturally derived **19**. - A solution of naturally derived **19** (3.5 mg) in $CDCl_3$ (0.3 ml) in an NMR tube was treated with trifluoroacetic acid (0.05 ml) resulting in rapid and quantitative conversion to the acetal **20**; $[\alpha]_D$ +3.0 (*c* 0.32, $CHCl_3$); 1H n.m.r. (200 MHz, $CDCl_3$ + trace of trifluoroacetic acid) δ 4.39 (1H, d, J 6.9 Hz, 3-H), 4.15 (1H, dd, J 4.0 Hz, 12.0 Hz, 1-H_b), 3.66 (1H, dd, J 0.6 Hz, 12.0 Hz, 1-H_a), 2.2 (2H, bm) and 1.9 (2H, bm, 4- and 5-H_2), 1.55 (3H, s, 6-CH_3), 1.50 (1H, bm, 2-H), 1.27 (3H, d, J 6.9 Hz, 2-CH_3); EIMS 142 (M^+, 3%), 112 (6), 101 (18), 83 (11), 67 (20), 55 (15), 43 (100); CIMS (NH_3) 143 $(M+H)^+$, 100%); HR(CI)MS 143.1073 ($[M+H]^+$ requires $C_8H_{15}O_2$ 143.1072).

Cyclisation of synthetically derived **19**. - Treatment of compound **19** (3.5 mg), derived synthetically, under the same conditions as above gave the acetal **20**; $[\alpha]_D$ +3.0 (*c* 0.30, $CHCl_3$) with similar ^1H n.m.r. and mass spectra to naturally derived **20**.

X-Ray Crystal Structure Analysis of (S,S*,S*)-[(η^5-C_5H_5)Fe(CO)(PPh_3)COCH(CH_3)CH(OCOPh)-$CH_2CH_2CH{=}CH_2$].* Cell parameters and reflections were measured using graphite monochromated Cu-Kα radiation on an Enraf Nonius CAD4-F diffractometer operating in ω/2θ mode. The scan range (ω) was calculated from [1.65 + 0.14 tanθ] and the scan speed was varied from 1.3 to 5.5° min^{-1} depending upon intensity. Reflections were measured in the range $0<\theta<70°$. Four standard reflections were measured regularly to scale the intensity data and correct for any crystal decay. The data were corrected for Lorentz, polarisation and absorption effects [26] and equivalent reflections were merged to give 6140 unique reflections of which 3376 were considered to be observed [$I>3\sigma(I)$] and used in the subsequent structure analysis. The structure was solved using direct methods and electron density Fourier synthesis.

Final full-matrix least squares refinement included parameters for atomic positions, anisotropic temperature factors (for non-hydrogen atoms), an overall scale factor and an extinction parameter.[27] All non hydrogen atoms were located in difference Fourier syntheses and hydrogen atoms were placed in calculated positions and allowed to "ride" on their respective atoms. Weights for each reflection were calculated from a Chebyshev series of the form $W=[17.381\ t_1(X) - 5.396t_2(X) + 12.603t_3(X)]$ where $X = F_o/F_{max}$.[28] Final difference Fourier synthesis showed no significant residual electron density. All calculations were performed using the CRYSTALS package on the Chemical Crystallography Laboratory VAX 11/750 computer.

Crystal Data.

$C_{39}H_{37}FeO_4P$, M=656.5397, monoclinic, a=21.711, b=8.197, c=19.118 , β=91.34°, U=3401.3 A^3, Z=4, D_{calc}=1.28 gcm^{-3}, μ(Cu-Kα)=43.14 cm^{-1}, space group $P2_{1/n}$, relative transmission factors 0.99-2.16, crystal dimensions 1.17x0.35x0.15 mm, number of relections [$I>3\sigma(I)$] 3376, R=0.059, R_w=0.069.

Acknowledgements: We thank B.P. International Limited for a Venture Research Award (to G.L.G. and M.W.) and the S.E.R.C. for support (to I.M.D-H.), and Dr Keith Prout for access to the facilities of the Chemical Crystallography Department, Oxford.

References

1. A. Horeau, "Stereocemistry, Fundamentals and Methods", vol. 3, Theime, Stuttgart, 1977, p.51.
2. R.J. Capon, J.K. MacLeod, *Tetrahedron* **41**, 3391 (1985).
3. M. Albericci, J.C. Braekman, D. Daloze, B. Tursch, *Tetrahedron* **38**, 1881 (1982).
4. Personal communication with Professor J.C. Braekman.
5. Numbering convention used throughout is that shown on the structure diagrams, first proposed in ref.1.
6. M. Albericci, M. Collart-Lempereur, J.C. Braekman, D. Daloze, B. Tursch, J.P. Declercq, G. Germain, M. van Meerssche, *Tetrahedron Lett.* 2687 (1979).
7. We thank Professor J.C. Braekman for a small sample of authentic sigmosceptrellin A.
8. It was based on this reasoning that a reappraisal and eventual reassignment[8] of absolute stereochemistries to the marine natural product ilimaquinone, together with a host of "correlated" compounds, was undertaken.
9. R.J. Capon, J.K. MacLeod, *J. Org. Chem.* **52**, 5059 (1987).
10. R.J. Capon, J.K. MacLeod, *J. Org. Chem.* **52**, 339 (1987).
11. R.J. Capon, J.K. MacLeod, *J. Nat. Prods.* **50**, 225 (1987).
12. S.G. Davies, I.M. Dorder-Hedgecock, P. Warner, *Tetrahedron Lett.* **26**, 2125 (1985).
13. Authentic 7 was obtained from the original specimen[1] of *Mycale (aegogrophila) c.f. ancorina* after methylation of the crude extract with diazomethane to facilitate purification by silica chromatography.

14. S.G. Davies, I.M. Dordor-Hedgecock, R.J.C. Easton, S.C. Preston, K.H. Sutton, J.C. Walker, *Bull Chim. Soc. Fr.* 608 (1987).

15. M. Whittaker, C.R. McArthur, C.C. Leznoff, *Can. J. Chem.* **63**, 2844 (1985).

16 a. L.S. Liebeskind, M.E. Welker, R.W. Fengl, *J. Am. Chem. Soc.* **108**, 6328 (1986).

b. S.G. Davies, I.M. Dordor-Hedgecock, P. Warner, R.H. Jones, K.J. Prout, *J. Organomet. Chem.* **285**, 213 (1985).

17. The iron acetyl complex $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)COCH_3]$ is available either as a racemate or enantiomerically pure (S)-(+) and (R)-(-) forms from B.P. Chemicals Ltd., New Specialities Business, Belgrave House, 76 Buckingham Palace Road, London, SW1W 0SU, U.K.

18. S.G. Davies, I.M. Dordor-Hedgecock, J.C. Walker, P. Warner, *Tetrahedon Lett.* **25**, 2709 (1984).

19 a. J.I. Seeman, S.G. Davies, *J. Am Chem. Soc.* **107**, 6522 (1985).

b. B.K. Blackburn, S.G. Davies, M. Whittaker, in "Stereochemistry of Organometallic and Inorganic Compounds", Ed. I. Bernal, vol. 3, Elsevier Science: Amsterdam, 1988.

c. G.J. Baird, S.G. Davies, R.H. Jones, K. Prout and P. Warner, *J.Chem. Soc., Chem. Commun.* 745 (1984).

d. D.E. Smith and J.A. Gladysz, *Organometallics*, **4**, 1480 (1985).

20. H.C. Brown, P.M. Weissman, *J. Am. Chem. Soc.* **87**, 5614 (1965).

21. J. Tsuji, *Synthesis*, 369 (1984).

22. The ^1H n.m.r. chemical shift for the C2-CH_3 in **12** could be expected to be *ca.* δ 1.25 ppm for an axial and *ca.* δ 0.70 ppm for an equatorial conformation.[2]

23. D.F. Shriver and M.A. Dresdon, "The Manipulation of Air-Sensitive Compounds", Wiley-Interscience, New York, 1986.

24. M. Green and D.J. Westlake, *J.Chem. Soc. A*, 1971, 367.

25. S. Abbott, G.J. Baird, S.G. Davies, I.M. Dordor-Hedgecock, T.R. Maberly, J.C. Walker and P. Warner, *J. Organomet. Chem.*, **289**, C13 (1985).

26. A.C.T. North, D.C. Philips and F.S. Mathews, *Acta Crystallogr. Sect. A*, **24**, 351 (1968).

27. A.C. Larson, "Crystallographic Computing", Ed. F.R. Ahmed, Munttsguard, 1970, p.170.

28. J.R. Carruthers and D.J. Watkin, *Acta Crystallogr. Sect. A*, **35**, 698 (1979).