Use of β-Sulfonyl Vinyl Ketones as Equivalents to Vinyl Ketones in Robinson Annelation. Convergent, Highly Stereoselective Preparation of a Hydrindanol Related to Vitamin D from 2-Methylcyclopent-2-enone and Lithiated (*E*)-But-2-enyldiphenylphosphine Oxide

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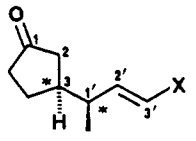
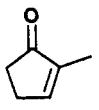
Conjugate addition of lithiated (*E*)-but-2-enyldiphenylphosphine oxide (**3**) to 2-methylcyclopent-2-enone (**2**) in tetrahydrofuran at −20 °C generates the enolate **8**, which reacts rapidly with a series of β-sulfonyl vinyl ketones to generate unsaturated diketones in good yields. Hydrogenation of the latter products under medium pressure followed by aldol ring closure of the resulting δ-diketones generates hydrindenones equivalent to those obtained by Robinson annelation. The hydrindenones are stereoselectively converted by diisobutylaluminum hydride in dichloromethane into β-hydrindenols. The functionalized hydrindenone **15** prepared by the foregoing method from the dioxanylethyl β-sulfonyl vinyl ketone **5**, upon hydrogenation under high pressure, gives with 95% stereoselectivity the *trans*-hydrindanone **20**. This is converted by the Horner–Wittig reaction with α-methacrolein into the diene **26**, hydrogenation of the β-epimer **26a** of which provides the hydrindanol **27** bearing the alkyl side chain and the correct relative configuration at C13, C14, C17, and C20 of vitamin D.

Introduction

The aprotic conjugate addition of lithiated (*E*)-but-2-enyl sulfoxides, phosphine oxides, phosphonates,[1,2] and sulfones[4] to 2-cyclopentenone proceeds rapidly at temperatures below 0 °C to give exclusively the adducts **1** in high yield. We describe here how the syn stereochemistry[2] of the adducts, which correlates with configuration at C17 and C20 of steroidal substrates, can be exploited to provide precursors of such compounds with correct relative configuration at C13, C17, and C20 *in one chemical operation*. As illustrated in Scheme I, the aprotic conjugate addition of the lithiated (*E*)-but-2-enyl carbanion to 2-methylcyclopent-2-enone (**2**) generates a lithium enolate, which reacts with an electrophile to give a cyclopentanone with the newly introduced substituents in a trans relationship. Although the use of enolate trapping involving the enone to set up the correct relative configuration at these centers has been described previously, the methods do not involve the direct conjugate additon of lithiated carbanions.[5] As the current conjugated addition reactions of the lithiated allylic sulfoxides and related reagents proceed so rapidly in the *absence* of special additives, their use in such a sequence is especially attractive.



1 X = SOR, $POPh_2$, $PO(OR)_2$, SO_2R



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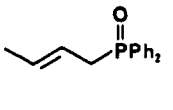

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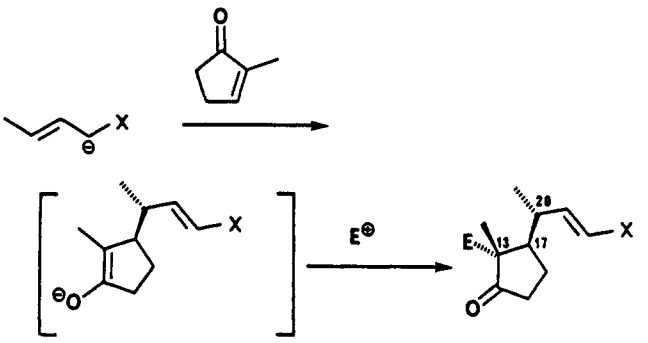
A successful realization of such a sequence, however, is critically reliant upon two factors. Firstly, the starting lithiated but-2-enyl carbanion must be stereochemically pure. Contamination with the *Z* isomer will result in formation of stereochemically undesirable anti products,[1-4] whose separation from the syn products is difficult. Of the (*E*)-but-2-enyl substrates so far prepared,[1-4] the diphenylphosphine oxide **3**[2] and the *p*-tolyl sulfone[4] are most easily recrystallized to geometric purity. As the phosphine oxide conveniently enables chain extension by way of Horner–Wittig reactions to be carried out in the latter stages of the synthesis, it was chosen in the present case. The second point relates to the enolate trapping. The electrophile, in providing the framework of the steroidal C ring, is logically an equivalent of methyl vinyl ketone or a homologue. However, because of polymerization under aprotic conditions, the use of alkyl vinyl ketones is rarely successful,[6] and modified reagents must be used.[7-9]

Scheme I



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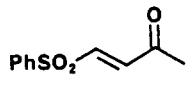
These generally are α-silyl[7] or α-thiovinyl ketones[8] whose preparation is not always straightforward for the lower homologues. An alternative means of preventing polymerization is to attach a leaving group to the β-position of the vinyl ketone such that the enolate is converted into a neutral unsaturated diketone by expulsion of the leaving group.[10] Full equivalence of the β-substituted vinyl ketone with methyl vinyl ketone is rendered through hydrogenation of the unsaturated diketone product to the δ-diketone required for aldol ring closure. Furthermore, a leaving group can be used that enhances the reactivity of the vinyl ketone toward the enolate. The development of such vinyl ketones bearing β-sulfonyl groups was carried out specifically for the enolate trapping described here.[10]

We now describe how four of these compounds, the β-sulfonyl vinyl ketones 4–7,[10] can be effectively used to trap the enolate arising by the conjugate addition of lithiated (*E*)-but-2-enyldiphenylphosphine oxide to the enone **2**. We describe the conversion of the adducts into hydrindenones bearing the correct relative configuration at C13, C17, and C20, and an exploratory conversion of one of the hydrindenones into a hydrindanol related to a precursor used in the synthesis of vitamin D. Part of this work has been described in a preliminary communication.[11]

Discussion

The deep-red lithiated carbanion of the phosphine oxide **3** in tetrahydrofuran (THF) at −60 °C was treated with the enone **2** until disappearance of the red color of the carbanion took place. The solution containing the enolate **8** was warmed to −20 °C, and then the vinyl ketone **4** was added. After 5 min, the mixture was quenched to provide



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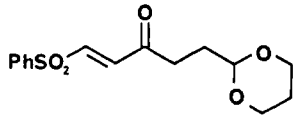

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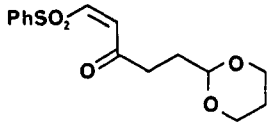

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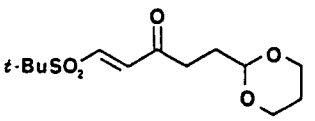

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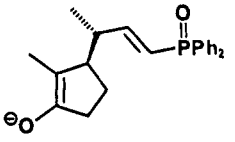

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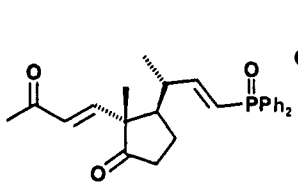
the unsaturated diketone **9** containing approximately 5% of the (*Z*)-enone in an overall isolated yield of 53% from the phosphine oxide **3**. Reaction of enolate **8** with the β-sulfonyl vinyl ketone **5** gave a 97:3 mixture of the adducts **10** and **11** (76% from the phosphine oxide). A slightly lower yield (67%) of the mixture, consisting almost entirely of the *E* adduct, was obtained when the β-*tert*-butylsulfonyl vinyl ketone **7** was used. Use of the (*Z*)-β-sulfonyl vinyl ketone **6** gave an equimolar mixture of the adducts **10** and **11** (54%). The *E* and *Z* isomers were obtained as single diastereomers. As the next step involved reduction of the double bonds, the formation of double-bond isomers was of no consequence. The efficiency of the enolate trapping with the β-sulfonyl vinyl ketones is noteworthy. By comparison, treatment of the enolate **8** with methyl α-(trimethylsilyl)vinyl ketone left approximately 75% of the enolate unreacted under the foregoing reaction conditions.



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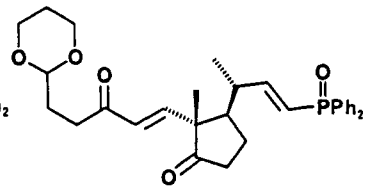

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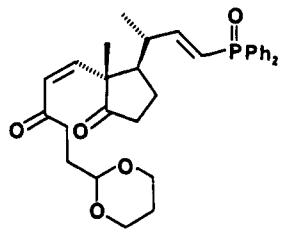

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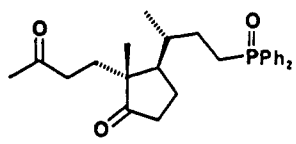
Hydrogenation of the unsaturated diketones to generate the saturated δ-diketones in the presence of palladium on charcoal under moderate pressure resulted in formation of epimers arising by double-bond migration in the vinylic phosphine oxide prior to hydrogenation. Double-bond migration is characteristic of highly active catalysts, particularly in relation to hydrogenation of Δ^7-steroidal alkenes,[12] but this can be suppressed through addition of pyridine.[13] Pyridine was also effective in suppressing bond migration in the present case, and hydrogenation of compound **9** in its presence yielded solely the δ-diketone **12** (98%). This compound in methanol containing 2% po-



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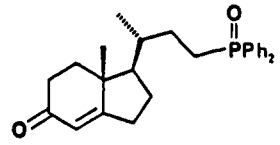

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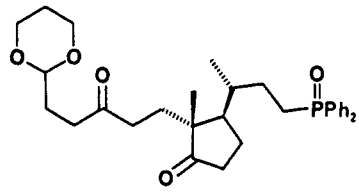

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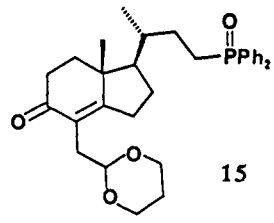

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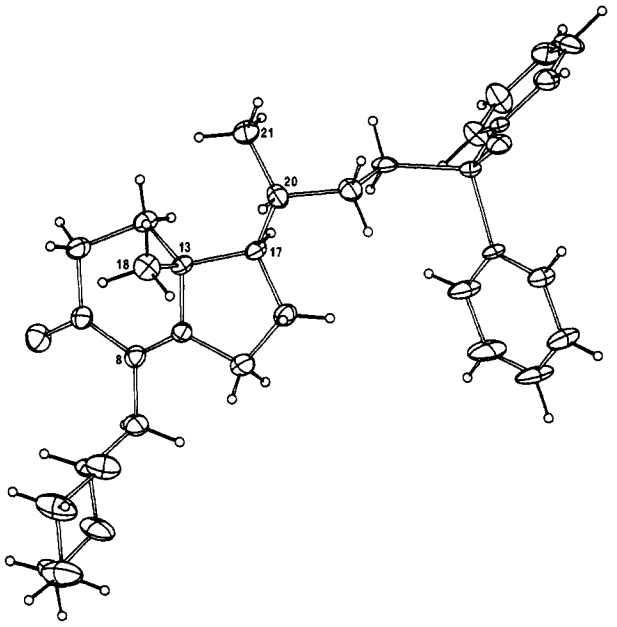
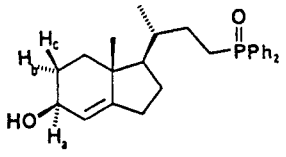


Figure 1. ORTEP plot of (1*RS*,1′*RS*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyl-1,2,3,6,7,7a-hexahydro-5*H*-inden-5-one (**15**).

tassium hydroxide was converted into the hydrindenone **13** in 82% yield, or 43% overall yield from the phosphine oxide **3**. Similarly, hydrogenation of the adduct **10** quantitatively gave the δ-diketone **14**, aldol ring closure of which gave the hydrindenone **15** (65% from the phosphine oxide **3**). The structure of the hydrindenone was unambiguously established by X-ray crystallographic analysis as given in the supplementary material. The ORTEP plot (Figure 1) clearly showed that the required configuration at C20 (steroid numbering) and the cis relationship between the side chain and the C18 methyl group had been secured.

In order to carry out the chain extension reactions on the hydrindenones, reduction of the carbonyl group was required. Hydrogenation of the double bond, either before or after chain extension, was also necessary. This is a crucial transformation, as this must provide a trans-fused hydrindan. Each compound was cleanly reduced with diisobutylaluminum hydride (DIBAL-H) in dichloromethane at −50 °C to the hydrindenols **16** and **17**, each in 75% yield. Acidic workup had to be avoided due to the



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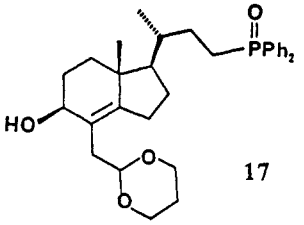

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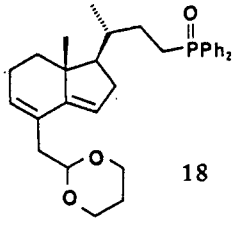

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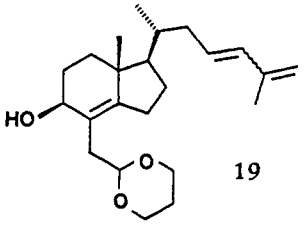

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extraordinary ease with which the hydrindenol **17** underwent dehydration to unstable diene **18**. The equatorial disposition of the hydroxyl group in the hydrindenols was indicated by the coupling constant of 6.6 Hz displayed by

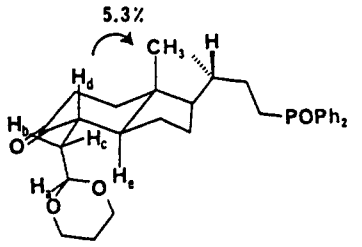

Figure 2. Preferred conformation of compound **20**.

protons H_a and H_b. Such a coupling is characteristic of an axial–equatorial relationship between these protons. Protons H_a and H_c with a coupling constant of 9.6 Hz are clearly diaxial.

The hydrindenol **16** is quite insoluble in most solvents, and the remaining synthetic work was more easily carried out with the hydrindenol **17**. It was intended to protect the hydroxyl group prior to the Horner–Wittig reaction as a bulky ether group such as a *tert*-butyldimethylsilyl ether. It was anticipated that the placement of a large group on the β-face of the compound would direct hydrogenation to the α-face to give the desired *trans*-hydrindanol. However, attempted silylation under forcing conditions[14] was unsuccessful. Initially, it was thought that the phosphinoyl group may have prevented the reaction, and so the Horner–Wittig reaction was performed on the unprotected hydrindenol. Reaction of the dianion of hydrindanol **17** in THF with α-methacrolein gave a mixture of β-hydroxy phosphine oxide diastereomers. These were converted by sodium hydride in *N*,*N*-dimethylformamide (DMF) at 70 °C into a 71:29 mixture of the (*E*)- and (*Z*)-dienes **19** in an overall yield of 31% from the hydrindenol. The reaction is discussed below. However, attempts to protect the hydroxyl group of the diene **19** were still unsuccessful. Without a means of protecting the hydroxyl group, the traditional approach of forming hydrindanones from hydrindenones by direct reduction had now to be used.

The problem encountered in the hydrogenation of steroidal hydrindenones is that because the angular methyl group tends to bias a conformational equilibrium toward a conformer possessing an exposed β-face,[15] hydrogenation takes place at that face to generate a *cis*-hydrindanone. However, the presence of a large β-subunit in the allylic position ensures predominance of a conformer with an exposed α-face, and hence α-hydrogenation, leading to trans fusion, ensues. Predominant formation of trans-fused hydrindanone systems also occurs with those substrates that either incorporate an extra fused ring, corresponding to the B ring of a steroid, which locks the CD rings into the conformation favored for α-hydrogenation,[16] or contain a carboxy group at C8 (steroid numbering) capable of hydrogen bonding to the carbonyl group such that the elements of a B ring are in place.[17] Other features that favor α-hydrogenation are the placement of a large group at C8, and a large β-substituent at C17.[18] The latter

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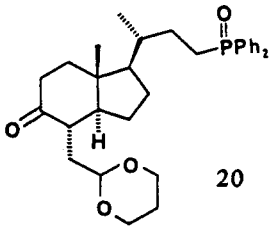
features are possessed by compound **15**. Hydrogenation of compound **15** under medium pressure (50–60 psi) was unacceptably slow, although this gave the *trans*-hydrindanones **20** and **21** and *cis*-hydrindanone **22**; the ratio of the trans to cis compounds was 80:20. Cleavage of the



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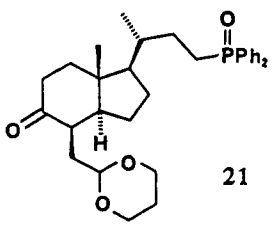

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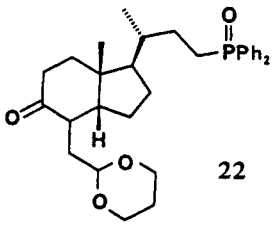

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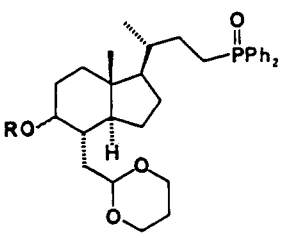
acetal group to give the aldehyde and other by products also took place. Addition of pyridine suppressed the formation of these byproducts and increased the amount of the 8β-epimer **21**. Hydrogenation at 600–900 psi was much more rapid and increased the ratio of trans to cis hydrindanones to 95:5. Treatment of the 75:25 mixture of α- and β-epimers of the *trans*-hydrindanone arising from the hydrogenation with sodium methoxide cleanly converted the β-epimer into the α-epimer **20**. Its structure (Figure 2) was confirmed by ^{1}H NMR spectroscopy. Irradiation of H_a (δ 4.747 ppm) enabled H_b (1.887 ppm) and H_c (1.418 ppm) to be located, and these were found to be coupled to H_d (2.542 ppm) by 9.7 and 2.8 Hz, respectively. A remaining coupling of 12.7 Hz in the H_d multiplet was attributed to a trans-diaxial coupling between H_d and H_e. This was consistent with a trans fusion and a preferred conformer with an equatorial substituent at C8 (Figure 2). In addition, preirradiation of H_d gave a 5.3% enhancement of the signal (at δ 0.960 ppm) from the angular methyl group. The hydrogenation experiment thus results in the selective introduction of a fourth stereogenic center with the correct relative configuration. The stereochemical outcome compares more than favorably with that obtained from the use of the 8-carboxy group to direct hydrogenation.[17]

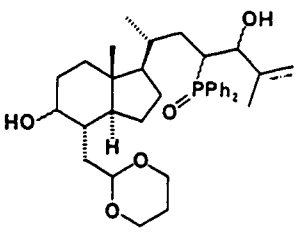
Reduction of the hydrindanone **20** with a large variety of hindered hydride donors gave mixtures of the β- and α-epimers of the hydrindanol **23**. The best selectivity was obtained with the DIBAL-H–2,6-di-*tert*-butyl-4-methylphenol reagent in toluene[19] at –60 °C, which gave a 91:9 mixture of the β- and α-epimers. However, a significant amount of an unidentified byproduct also formed. The reduction was most easily performed with DIBAL-H in dichloromethane at –70 °C, and this proceeded rapidly to give a 79:21 mixture of the epimers in 79% yield. While higher stereoselectivity is desirable at this stage, it is emphasized that, within the context of the synthesis of vitamin D precursors, stereochemical information at C9 will ultimately be lost.

Protection of the hydroxyl group in hydrindanol **23**, as in the case of compounds **17** and **19**, was again difficult. As a bulky protecting group was now unnecessary, a methyl group was considered to be sufficient. However, under standard conditions,[20] a very slow formation of the methyl ether **24** took place in low yield (50%); unchanged hydrindanol (26%) was also recovered. In view of the inef-



23 R = H

24 R = Me



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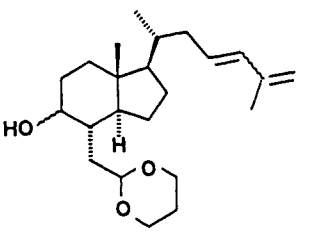

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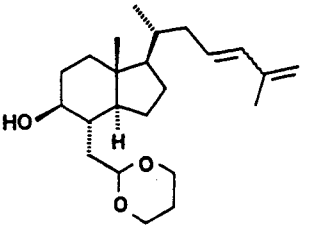
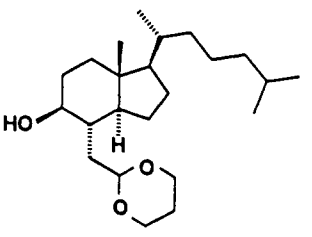


26a



27

ficiency of the protection, the elaboration of the side chain was carried out with the dianion of the hydrindanol. This was treated with α-methacrolein in THF at low temperature to give the β-hydroxy phosphine oxide **25** as a mixture of diastereomers in 70% yield. Also recovered was unreacted hydrindanol **23** (16%). The β-hydroxy phosphine oxide mixture was treated with sodium hydride in DMF at 70 °C to give both a 74:26 mixture of the (*E*)- and (*Z*)-diene isomers **26** (40% from the hydrindanol **23**) and the hydrindanol **23** (32%). Erythro β-hydroxy phosphine oxides, generally the major products of the reaction of aldehydes with lithiated phosphine oxides, give (*Z*)-alkenes, whereas threo β-hydroxy phosphine oxides give (*E*)-alkenes.[21] However, elimination of diphenylphosphinite from the alkoxide of an erythro adduct proceeds more slowly than its elimination from threo alkoxide.[21] A second competing reaction, that of dissociation, thus becomes important for the erythro adduct. If recombination takes place, an equilibrium situation arises wherein newly formed threo adduct will eventually lead to (*E*)-alkene. However, if recombination is disfavored, then a large amount of the erythro adduct will be converted into dissociation products. This appears to be the case both here

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and in the formation of compound **19**. Addition of methacrolein was carried out under conditions that favor formation of the erythro β-hydroxy phosphine oxides,[21] and yet, of the dienes formed in the next step, these were predominantly of *E* geometry. Thus, the dissociation to give the hydrindanol **23** occurs via the erythro adduct. Such dissociation appears to be prevalent among the adducts derived from aromatic aldehydes.[21] Whether the α,β-unsaturation of α-methacrolein is a contributing factor in the above case needs to be established.[22]

The β-hydroxy epimers **26a** of the diene mixture were isolated and were quantitatively hydrogenated at atmospheric pressure to give the saturated product **27**.

Conclusion

The preparation of the hydrindanol **23** in five steps in an overall yield of 43% from the allylic phosphine oxide represents an efficient utilization of the conjugate addition of a lithiated allylic carbanion in a stereoselective synthetic scheme. From this work has emerged the use of β-sulfonyl vinyl ketones as efficient enolate trapping reagents, and it is this that has caused the preparation of the hydrindanol to be highly convergent and direct. It is clear that hydrindanols related to compound **23** will be useful synthons for the construction of metabolites of vitamin D. The introduction of the vitamin D side chain as demonstrated by the preparation of the hydrindanol **27** is illustrative of this, although it is emphasized that the preparation was conducted at the exploratory level. As dissociation of the intermediate phosphine oxides interferes with the use of the Horner–Wittig reaction for the chain extension, both the nonallylic groups on the phosphorus, and the aldehyde, must be varied so as to depress the tendency for dissociation to occur. Clearly, threo selectivity in the reaction needs also to be enhanced. However, the sequence does illustrate how conveniently the phosphine oxide can be used for chain extension.

The ultimate aim of the work is to prepare optically pure target compounds. According to the transition-state model of the reaction,[1,2] it is the configuration at phosphorus that will determine the face selectivity of the reaction of the lithiated reagent with the enone. To ensure complete face selectivity, the required optically active but-2-enylphosphine oxide must have two different nonallylic substituents that have substantially different steric requirements.[2,23] The *E* geometry will provide the required syn selectivity. Once these conditions are met, then the preparation of a series of precursors to the CD portions of the structurally diverse metabolites of vitamin D from the one optically active phosphine oxide should then be possible. The methodology described herein has the potential of providing such compounds in a considerably more straightforward fashion than that hitherto described.[25]

Experimental Section

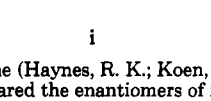
General Aspects. Melting points were recorded on a Reichert melting point stage and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker WM400 (400 MHz) spectrometer, with samples dissolved in $CDCl_3$. IR spectra were recorded on Perkin-Elmer 221 and 710B spectrometers or a Digilab FTS 20/80 Fourier transform spectrometer from solutions in $CHCl_3$. Mass spectroscopy was carried out on an AEI MS9 spectrometer with a DS30 data handing system for high-resolution spectra. Microanalyses were performed by the Australian Mineral Development Laboratories, Melbourne. The composition of diastereomeric mixtures was determined by 400-MHz ^{1}H NMR spectroscopy. Chromatographic separations were carried out by flash chromatography with Merck silica gel 60 (230–400 mesh, ASTM). Merck silica gel (60 PF_{254}) was used for preparative centrifugal (radial) chromatography with a Chromatotron Model 7924 instrument, Harrison Research U.S.A. Analytical TLC was carried out with Merck precoated aluminum TLC plates coated with silica gel 60 F 254 (0.2 mm). HPLC was carried out on a Waters 6000 analytical instrument equipped with a refractive index detector and UV detector. The precise conditions used for individual compounds are given below.

THF was dried over sodium and then stored over sodium and sodium hydride in the presence of benzophenone under nitrogen. Immediately prior to use, it was distilled into the reaction vessel under nitrogen. Butyllithium as a solution in hexane was standardized by titration against 2,5-dimethoxybenzyl alcohol.[26] Other solvents and commercially available reagents were purified in the standard manner.[27] 2-Methylcyclopent-2-enone (**2**) was prepared according to a literature method.[28] The preparation of the phosphine oxide **3**[2] and the sulfones **4**–**7**[12] is described elsewhere.

Enolate Trapping with the Sulfones 4–7. With (*E*)-4-(Phenylsulfonyl)but-3-en-2-one (4). Butyllithium was added dropwise to a stirred solution of (*E*)-but-2-enyldiphenylphosphine oxide (**3**) (394 mg, 1.54 mmol) in THF (20 mL) at −60 °C until the first permanent orange color due to the anion appeared (this operation removed traces of protic impurities, and typically, <0.1 mL of butyllithium was required). More butyllithium (0.65 mL, 1.61 mmol, 2.49 M in hexane) was added at −60 °C to effect complete deprotonation. The resulting red-orange solution was stirred for a further 10 min and then treated dropwise with a solution of the enone **2** (155 mg, 1.61 mmol) in THF (2 mL) such that the temperature remained between −75 and −70 °C. The reaction mixture was then warmed to −20 °C, and a solution of the sulfone **4** (484 mg, 2.30 mmol) in THF (6 mL) was added dropwise so as to maintain the reaction temperature between −20 and −15 °C. During the addition, the solution acquired an orange-red color. Stirring was continued within the above temperature range for 5 min, and then reaction mixture was quenched with saturated aqueous ammonium chloride (10 mL). The resulting mixture was extracted with ethyl acetate, and the extracts were washed with brine, dried (Na_2SO_4), and evaporated under reduced pressure to leave an orange viscous oil. This was immediately submitted to flash chromatography with 1:24 methanol–ethyl acetate followd by radial chromatography[29] to give (**1′*RS*,1″*E*,2*SR*,2′*E*,3*SR***)-3-[3′-(diphenylphosphinoyl)-1′-

(22) Use of isobutyraldehyde gives largely unchanged starting materials, possibly through protonation of the dianion by the aldehyde.

(23) In this regard, the *racemic* lithiated (*E*)-but-2-enyl-*tert*-butylphenylphosphine oxide i undergoes completely stereoselective conjugate



i

addition to cyclopentenone (Haynes, R. K.; Koen, M., unpublished work, 1986). We have also prepared the enantiomers of i and will report on the reactions of the lithiated reagents elsewhere. It is worth noting that Hua and co-workers[24] prepared a number of chiral allyl (prop-2-enyl) oxazaphospholidene oxides and found that these reagents underwent highly diastereoselective conjugate addition to cyclic enones providing the nitrogen atom bore a relatively bulky isopropyl substituent.

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(29) Enolate trapping with the β-sulfonyl vinyl ketone was accompanied by the formation of a yellow byproduct, which tended to coelute with the main product during chromatographic purification. If the ethyl acetate extracts of the crude product were left to stand for 2 days, then decomposition of the yellow material to baseline material took place, thus obviating the use of a second chromatographic purification. The nature of this byproduct was not established, but it presumably arises from the eliminated phenylsulfinate.

methylprop-2′-enyl]-2-methyl-2-(3″-oxobut-1″-enyl)cyclopentan-1-one (9), containing 5% of the 1′*RS*,1″*Z*,2*SR*,2′*E*,3*SR* isomer, as a brittle foam (340 mg, 53%) after throrough drying at high vacuum. Trituration with ether of the highly viscous oil obtained after preliminary evaporation of the solvents aided in releasing trapped solvent. The minor isomer could not be removed by HPLC. ^{1}H NMR [(*) denotes the 1″*Z* isomer]: δ 1.011* (3 H, d, $J_{1'\text{-Me},1'}$ = 6.6 Hz, 1′-CH_3), 1.057 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.6 Hz, 1′-CH_3), 1.135* (3 H, s, 2-CH_3), 1.145 (3 H, s, 2-CH_3), 1.586 (1 H, dddd, $J_{4\beta,4\alpha}$ = 12, $J_{4\beta,3\alpha}$ = 12, $J_{4\beta,3}$ = 11.6, $J_{4\beta,5\beta}$ = 8.4 Hz, H4β), 2.03–2.13 (1 H, m, H4α), 2.153 (1 H, ddd, $J_{3,4\beta}$ = 11.8, $J_{3,2'}$ = 9.5, $J_{3,4\alpha}$ = 6.0 Hz, H3), 2.255 (1 H, ddd,$J_{5\alpha,5\beta}$ = 19.5, $J_{5\alpha,4\beta}$ = 12, $J_{5\alpha,4\alpha}$ = 9 Hz, H5α), 2.26 (3 H, s, H4″), 2.470 (1 H, dd, $J_{5\beta,5\alpha}$ = 19.5, $J_{5\beta,4\beta}$ = 8.5 Hz, H5β), 2.518 (1 H, ddq, $J_{1',3}$ = 9.5, $J_{1',3'}$ = 8.5, $J_{1',1'\text{-Me}}$ = 6.6 Hz, H1′), 5.948* (1 H, d, $J_{2'',1''}$ = 11.5 Hz, H2″), 6.186 (1 H, d, $J_{2'',1''}$ = 16.5 Hz, H2″), 6.303 (1 H, ddd, $J_{3',P}$ = 24.5, $J_{3',2'}$ = 17, $J_{3',1'}$ = 0.8 Hz, H3′), 6.663 (1 H, d, $J_{1'',2''}$ = 16.5 Hz, H1″), 6.682 (1 H, ddd, $J_{2',P}$ = 19.5, $J_{2',3'}$ = 17, $J_{2',1'}$ = 9 Hz, H2′), 7.45–7.59 (6 H, m, C_6H_5 meta, para), 7.65–7.74 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{26}H_{29}O_3P$ 420.1854, found 420.1854.

With (*E*)-5-(1′,3′-Dioxan-2′-yl)-1-(phenylsulfonyl)pent-1-en-3-one (5). The conjugate addition–enolate trapping sequence was carried out as described above with the phosphine oxide **3** (371 mg, 1.45 mmol), butyllithium (0.58 mL, 1.45 mmol, 2.5 M in hexane), the enone **2** (139 mg, 1.45 mmol), and the sulfone **5** (540 mg, 1.74 mmol). The product was extracted into ethyl acetate. The combined extracts were washed with brine, dried (Na_2SO_4), and left to stand for 2 days, by which time TLC indicated the formation of yellow baseline material derived from the eliminated phenylsulfinate.[29] Evaporation of the solvents followed by flash chromatography with 1:24 methanol–ethyl acetate of the resulting yellow oil gave **(1′*RS*,1″*E*,2*SR*,2′*E*,3*SR*)-2-[5″-(1‴,3‴-dioxan-2‴-yl)-3″-oxopent-1″-enyl]-3-[3′-(diphenylphosphinoyl)-1′-methylprop-2′-enyl]-2-methylcyclopentanone (10)**, containing 3% of the 1′*RS*,1″*Z*,2*SR*,2′*E*,3*SR* isomer **11**, as a brittle foam (574 mg, 76%). ^{1}H NMR: δ 1.045 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.2 Hz, 1′-CH_3), 1.130 (3 H, s, 2-CH_3), 1.326 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.2, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.4, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.2 Hz, H5‴α), 1.573 (1 H, dq, $J_{4\beta,4\alpha}$ = $J_{4\beta,3}$ = $J_{4\beta,5\alpha}$ = 12, $J_{4\beta,5\beta}$ = 8.4 Hz, H4β), 1.910 (2 H, dt, $J_{5'',4''}$ = 7.2, $J_{5'',2'''}$ = 4.8 Hz, H5″), 1.99–2.11 (2 H, m, H4α, H5‴β), 2.145 (1 H, ddd, $J_{3,4\beta}$ = 12.0, $J_{3,2'}$ = 9.6, $J_{3,4\alpha}$ = 6.0 Hz, H3), 2.245 (1 H, ddd, $J_{5\alpha,5\beta}$ = 19.2, $J_{5\alpha,4\beta}$ = 12, $J_{5\alpha,4\alpha}$ = 9 Hz, H5α), 2.453 (1 H, dd, $J_{5\beta,5\alpha}$ = 19.2, $J_{5\beta,4\beta}$ = 8.4 Hz, H5β), 2.503 (1 H, ddq, $J_{1',3}$ = 9.6, $J_{1',2'}$ = 8.4, $J_{1',1'\text{-Me}}$ = 6.2 Hz, H1′), 2.695 (2 H, t, $J_{4'',5''}$ = 7.2 Hz, H4″), 3.69–3.79 (2 H, m, H4‴α, H6‴α), 4.04–4.11 (2 H, m, H4‴β, H6‴β), 4.585 (1 H, t, $J_{2''',5'''}$ = 4.8 Hz, H2‴), 6.195 (1 H, d, $J_{2'',1''}$ = 16.3 Hz, H2″), 6.294 (1 H, dd, $J_{3',P}$ = 24.5, $J_{3',2'}$ = 17 Hz, H3′), 6.673 (1 H, ddd, $J_{2',P}$ = 19, $J_{2',3'}$ = 17, $J_{2',1'}$ = 8.5 Hz, H2′), 6.695 (1 H, d, $J_{1'',2''}$ = 16.3 Hz, H1″), 7.44–7.59 (6 H, m, C_6H_5 meta, para), 7.66–7.74 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{31}H_{37}O_5P$ 520.2378, found 520.2365.

With (*Z*)-5-(1′,3′-Dioxan-2′-yl)-1-(phenylsulfonyl)pent-1-en-3-one (6). The conjugate addition–enolate trapping was carried out with the phosphine oxide **3** (338 mg, 1.32 mmol), butyllithium (0.58 mL, 1.45 mmol), the enone **2** (126 mg, 1.32 mmol), and the sulfone **6** (491 mg, 1.58 mmol). The usual workup gave a foam (371 mg, 54%) consisting of a 1:1 mixture of the adduct **10** and the 1′*RS*,1″*Z*,2*SR*,2′*E*,3*SR* isomer **11**. The mixture was submitted to HPLC with 3:197 methanol–ethyl acetate (Whatman Partisil M9 column, 4.0 mL/min, 1200 psi) to give **(1′*RS*,1″*Z*,2*SR*,2′*E*,3*SR*)-2-[5″-(1‴,3‴-dioxan-2‴-yl)-3″-oxopent-1″-enyl]-3-[3′-(diphenylphosphinoyl)-1′-methylprop-2′-enyl]-2-methylcyclopentanone (11)** (t_R 29 min) as a solid foam followed by the adduct **10** (t_R 39.3 min). ^{1}H NMR: δ 1.004 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.5 Hz, 1′-CH_3), 1.126 (3 H, s, 2-CH_3), 1.304 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.3, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.4, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.2 Hz, H5‴α), 1.483 (1 H, dddd, $J_{4\beta,4\alpha}$ = 13, $J_{4\beta,3}$ = $J_{4\beta,5\alpha}$ = 11.6, $J_{4\beta,5\beta}$ = 9.6 Hz, H4β), 1.835 (2 H, dt, $J_{5'',4''}$ = 7.3, $J_{5'',2'''}$ = 4.9 Hz, H5″), 2.027 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.4, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.6, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 4.9 Hz, H5‴β), 2.03–2.11 (1 H, m, H4α), 2.360 (1 H, ddd, $J_{5\beta,5\alpha}$ = 19, $J_{5\beta,4\beta}$ = 9.5, $J_{5\beta,4\alpha}$ = 1.1 Hz, H5β), 2.38–2.46 (1 H, m, H1′), 2.52–2.59 (1 H, m, H3), 2.54–2.59 (2 H, m, H4″), 2.775 (1 H, ddd, $J_{5\alpha,5\beta}$ = 19, $J_{5\alpha,4\beta}$ = 11.4, $J_{5\alpha,4\alpha}$ = 9.9 Hz, H5α), 3.69–3.78 (2 H, m, H4‴α, H6‴α), 4.02–4.09 (2 H, m, H4‴β, H6‴β), 4.518 (1 H, t, $J_{2''',5'''}$ = 5.0 Hz, H2‴), 5.919 (1 H, d, $J_{2'',1''}$ = 11.9 Hz, H2″), 6.210 (1 H, d, $J_{1'',2''}$ = 11.9 Hz, H1″), 6.253 (1 H, dd, $J_{3',P}$ = 23.3, $J_{3',2'}$ = 16.9 Hz, H3′), 6.512 (1 H, ddd, $J_{2',P}$ = 19.3, $J_{2',3'}$ = 16.9, $J_{2',1'}$ = 8.5 Hz, H2′), 7.44–7.57 (6 H, m, C_6H_5 meta, para), 7.65–7.73 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{31}H_{37}O_5P$ 520.2378, found 520.2365.

With (*E*)-1-(*tert*-Butylsulfonyl)-5-(1′,3′-dioxan-2′-yl)-pent-1-en-3-one (7). The conjugate addition–enolate trapping was carried out with the phosphine oxide **3** (346 mg, 1.35 mmol), butyllithium (0.59 mL, 1.48 mmol, 2.5 M in hexane), the enone **2** (143 mg, 1.48 mmol), and the sulfone **7** (470 mg, 1.62 mmol). The adduct was isolated as previously described as a foam (470 mg, 67%) and as predominantly the 1′*RS*,1″*E*,2*SR*,2′*E*,3*SR* isomer **10**.

Preparation of Hydrindenones. From the Diketone 9. The unsaturated diketone **9** (216 mg, 0.51 mmol) was dissolved in ethyl acetate (20 mL) containing pyridine (4 drops, ca. 0.02 mL) and then agitated with 10% palladium on charcoal (20 mg) under a hydrogen atmosphere at 35 psi (2.4 atm) for 24 h. Filtration of the catalyst and evaporation of the solvent left a solid, which was submitted to flash chromatography with ethyl acetate and then 1:49 methanol–ethyl acetate to give **(1′*RS*,2*RS*,3*RS*)-3-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-2-methyl-2-(3″-oxobutyl)cyclopentan-1-one (12)** as a white powder (214 mg, 98%), mp 133–135 °C, from ether. HPLC analysis with 3:197 methanol–ethyl acetate (Waters semipreparative μ-Porasil column, 3 mL/min, 900 psi, t_R 29.8 min) showed this to be >95% pure. ^{1}H NMR: δ 0.853 (3 H, s, 2-CH_3), 1.012 (3 H, d, $J_{1',2'}$ = 6.5 Hz, 1′-CH_3), 1.33–1.51 (2 H, m, H2′, H4β), 1.639 (1 H, ddqd, $J_{1',2'}$, = $J_{1',3'}$ = 8.8, $J_{1',1'\text{-Me}}$ = 6.5, $J_{1',2'}$ = 2.7 Hz, H1′), 1.723 (1 H, ddd, $J_{1'',1''}$ = 14.5, $J_{1'',2''}$ = 11.3, $J_{1'',2''}$ = 5.5 Hz, H1″), 1.723 (1 H, ddd, $J_{3,4}$ = 11.3, $J_{3,1'}$ = 8.8, $J_{3,4}$ = 6.0 Hz, H3), 1.850 (1 H, ddddd, $J_{2',P}$ = 13, $J_{2',2'}$ = 13, $J_{2',3'}$ = 8.2, $J_{2',3'}$ = 4.8, $J_{2',1'}$ = 2.7 Hz, H2′), 1.959 (1 H, ddd, $J_{1'',1''}$ = 14.6, $J_{1'',2''}$ = 11.2, $J_{1'',2''}$ = 5.0 Hz, H1″), 1.97–2.06 (2 H, m, H4α, H5α), 2.09–2.18 (1 H, m, H3′), 2.109 (3 H, s, H4″), 2.202 (1 H, ddd, $J_{2'',2''}$ = 16.2, $J_{2'',1''}$ = 10.9, $J_{2'',1''}$ = 5.0 Hz, H2″), 2.27–2.38 (2 H, m, H3′, H5β), 2.417 (1 H, ddd, $J_{2'',2''}$ = 16.2, $J_{2'',1''}$ = 10.9, $J_{2'',1''}$ = 5.0 Hz, H2″), 7.46–7.57 (6 H, m, C_6H_5 meta, para), 7.72–7.79 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{26}H_{33}O_3P$ 424.2167, found 424.2170.

The diketone **12** (350 mg, 0.82 mmol) in a solution of potassium hydroxide in methanol (2%, 15 mL) was stirred under gentle reflux for 2 h. The reaction mixture was cooled, saturated ammonium chloride solution (5 mL) was added, and the methanol was then removed by evaporation under reduced pressure. Ether–dichloromethane (2:1, 75 mL) and saturated ammonium chloride solution (5 mL) were added to the heterogeneous residue, and then the whole was shaken and separated. The organic layer was washed with brine and dried (Na_2SO_4), and the solvents were evaporated under reduced pressure to leave an orange viscous oil. **(1*RS*,1′*RS*,7a*RS*)-1-[3′-(Diphenylphosphinoyl)-1′-methylpropyl]-7a-methyl-1,2,3,6,7,7a-hexahydro-5*H*-inden-5-one (13)** was then isolatd by flash chromatography with 3:97 methanol–ethyl acetate as a colorless viscous oil. This was triturated with ether and dried thoroughly under high vacuum to afford a white brittle foam (274 mg, 82%). An analytical sample was obtained by HPLC with 1:24 methanol–ethyl acetate (Whatman Partisil 10 M20 column, 13 mL/min, 600 psi, t_R 35.5 min). ^{1}H NMR: δ 1.000 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.8 Hz, 1′-CH_3), 1.044 (3 H, s, 7a-CH_3), 1.34–1.52 (3 H, m, H1, H2β, H2′), 1.62–1.71 (1 H, m, H1′), 1.77–1.93 (2 H, m, H2α, H2′), 1.813 (1 H, ddd, $J_{7\alpha,6\beta}$ = 14.4, $J_{7\alpha,7\beta}$ = 13.5, $J_{7\alpha,6\alpha}$ = 4.9 Hz, H7α), 2.156 (1 H, dddd, $J_{3',P}$ = 14.5, $J_{3',3'}$ = 12, $J_{3',2'}$ = 12, $J_{3',2'}$ = 4 Hz, H3′), 2.206 (1 H, ddd, $J_{7\beta,7\alpha}$ = 13.5 $J_{7\beta,6\beta}$ = 5.1, $J_{7\beta,6\alpha}$ = 1.8 Hz, H7β), 2.25–2.39 (3 H, m, H3β, H3′, H6α), 2.514 (1 H, ddd, $J_{6\beta,6\alpha}$ = 17.8, $J_{6\beta,7\alpha}$ = 14.4, $J_{6\beta,7\beta}$ = 5.1 Hz, H6β), 2.593 (1 H, dddd, $J_{3\alpha,3\beta}$ = 19.9, $J_{3\alpha,2}$ = 10.6, $J_{3\alpha,2}$ = 2.4, $J_{3\alpha,4}$ = 2.1 Hz, H3α), 5.723 (1 H, br s, $W_{h/2}$ = 4.4 Hz, H4), 7.46–7.57 (6 H, m, C_6H_5 meta, para), 7.73–7.79 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{26}H_{31}O_2P$ 406.2061, found 406.2063.

From the Diketone 10. The diketone **10** was prepared from the phosphine oxide **3** (904 mg, 3.53 mmol), butyllithium (1.41 mL, 3.53 mmol, 2.5 M in hexane), the enone **2** (373 mg, 4.23 mmol), and the sulfone **5** (1.314 g, 4.24 mmol). The resulting foam (1.548 g) obtained after flash chromatography of the crude product was dissolved in ethyl acetate (40 mL) containing pyridine (8 drops, ca. 0.04 mL), and the whole was shaken with 10% palladium on charcoal (150 mg) under a hydrogen atmosphere at 38 psi (2.6

atm) for 22 h. Removal of the catalyst by filtration followed by evaporation of the solvent left the crude product, **(2*RS*,2′*RS*,3*RS*)-2-[5‴-(1‴,3‴-dioxan-2‴-yl)-3‴-oxopentyl]-3-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-2-methylcyclopentanone (14)**, as a viscous oil. ^{1}H NMR: δ 0.842 (3 H, s, 2-CH_3), 1.007 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.5 Hz, 1′-CH_3), 1.312 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.5, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.6, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.3 Hz, H5‴α), 1.34–1.50 (2 H, m, H2′, H4β), 1.632 (1 H, dtq, $J_{1',2'}$ = $J_{1',3}$ = 9.1, $J_{1',1'\text{-Me}}$ = 6.7, $J_{1',2'}$ = 2.8 Hz, H1′), 1.719 (1 H, ddd, $J_{3,4}$ = 11.6, $J_{3,1'}$ = 9.1, $J_{3,4}$ = 6.0 Hz, H3), 1.725 (1 H, ddd, $J_{1'',1''}$ = 14.4, $J_{1'',2''}$ = 11.0, $J_{1'',2''}$ = 5.0 Hz, H1″), 1.81–1.87 (2 H, m, H5″), 1.951 (1 H, ddd, $J_{1'',1''}$ = 14.3, $J_{1'',2''}$ = 11.0, $J_{1'',2''}$ = 5.0 Hz, H1″), 1.96–2.05 (2 H, m, H4α, H5α), 2.029 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.4, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.6, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 5.0 Hz, H5‴β), 2.12–2.21 (1 H, m, H3′), 2.184 (1 H, ddd, $J_{2'',2''}$ = 16.2, $J_{2'',1''}$ = 11.2, $J_{2'',1''}$ = 5.0 Hz, H2″), 2.26–2.38 (2 H, m, H3′, H5β), 2.390 (1H, ddd, $J_{2'',2''}$ = 16.2, $J_{2'',1''}$ = 11.2, $J_{2'',1''}$ = 5.0 Hz, H2″), 2.47–2.52 (2 H, m, H4″), 3.69–3.76 (2 H, m, H4‴α, H6‴α), 4.03–4.09 (2 H, m, H4‴β, H6‴β), 4.538 (1 H, t, $J_{2''',5'''}$ = 4.9 Hz, H2‴), 7.45–7.57 (6 H, m, C_6H_5 meta, para), 7.72–7.79 (4 H, m, C_6H_5 ortho).

The crude product was immediately dissolved in a solution of potassium hydroxide in methanol (2%, 40 mL), heated under gentle reflux for 2 h, and worked up as in the preceding case. Flash chromatography with 1:49 methanol–ethyl acetate of the crude material afforded **(1*RS*,1′*RS*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyl-1,2,3,6,7,7a-hexahydro-5*H*-inden-5-one (15)** as a brittle foam (1.161 g, 65% from the phosphine oxide) after thorough drying under high vacuum. An analytical sample was obtained as prisms, mp 148–150 °C, from ethyl acetate. The X-ray crystallographic analysis of this compound is given in the supplementary material. ^{1}H NMR: δ 0.998 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.7 Hz, 1′-CH_3), 1.014 (3 H, s, 7a-CH_3), 1.268 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.5, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.6, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.3 Hz, H5‴α), 1.36–1.52 (3 H, m, H1, H2α, H2′), 1.653 (1 H, ddd, $J_{1',1}$ = $J_{1',2'}$ = 8.5, $J_{1',1'\text{-Me}}$ = 6.7, $J_{1',2'}$ = 3 Hz, H1′), 1.814 (1 H, dt, $J_{7\alpha,6\beta}$ = 13.8, $J_{7\alpha,7\beta}$ = 13.0, $J_{7\alpha,6\alpha}$ = 5.0 Hz, H7α), 1.79–1.89 (2 H, m, H2β, H2′), 2.019 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.4, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.6, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 5.0 Hz, H5‴β), 2.159 (1 H, ddt, $J_{3',P}$ = 14.6, $J_{3',3'}$ = 12.2, $J_{3',2'}$ = 12.2, $J_{3',2'}$ = 4.3 Hz, H3′), 2.166 (1 H, ddd, $J_{7\beta,7\alpha}$ = 13.0, $J_{7\beta,6\beta}$ = 5.4, $J_{7\beta,6\alpha}$ = 2.3 Hz, H7β), 2.26–2.35 (1 H, m, H3′), 2.344 (1 H, ddd, $J_{3\alpha,3\beta}$ = 18.0, $J_{3\alpha,2\alpha}$ = 5.1, $J_{3\alpha,1}$ = 1.9 Hz, H3α), 2.426 (1 H, dd, $J_{1''\alpha,1''\beta}$ = 13.5, $J_{1''\alpha,2'''}$ = 5.5 Hz, H1″α), 2.459 (1 H, dd, $J_{1''\beta,1''\alpha}$ = 13.5, $J_{1''\beta,2'''}$ = 5.5 Hz, H1″β), 2.48–2.63 (2 H, m, H6), 2.550 (1 H, ddd, $J_{3\beta,3\alpha}$ = 18.0, $J_{3\beta,2\alpha}$ = 14.0, $J_{3\beta,2\beta}$ = 5.4 Hz, H3β), 3.63–3.71 (2 H, m, H4‴α, H6‴α), 3.99–4.04 (2 H, m, H4‴β, H6‴β), 4.590 (1 H, t, $J_{2''',1''}$ = 5.5 Hz, H2‴), 7.45–7.56 (6 H, m, C_6H_5 meta, para), 7.72–7.79 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{31}H_{39}O_4P$ 506.2585, found 506.2586.

Preparation of Hydrindenols. From the Hydrindenone 13. A stirred solution of the hydrindenone **13** (678 mg, 1.67 mmol) in dichloromethane (16 mL) was treated with DIBAL-H (2.85 mL, 5.0 mmol, 25% solution in toluene) at −50 °C under nitrogen. TLC analysis showed that the reaction took place immediately. The reaction mixture was warmed to 15 °C and quenched with saturated aqueous sodium sulfate solution. The resulting mixture was stirred for 20 min, during which time precipitation of aluminum salts took place. The solid material was removed by filtration, and the organic phase was separated and dried (Na_2SO_4). Evaporation of the solvent left a pale viscous oil (663 mg), which was submitted to flash chromatography with 1:49 methanol–ethyl acetate to give **(1*RS*,1′*RS*,5*SR*,7a*RS*)-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyl-2,3,5,6,7,7a-hexahydro-1*H*-inden-5-ol (16)** as a white powder (510 mg, 75%), mp 195–197.5 °C, from ether. ^{1}H NMR: δ 0.925 (3 H, s, 7a-CH_3), 0.950 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.7 Hz, 1′-CH_3), 1.154 (1 H, ddd, $J_{1,2\alpha}$ = 11.1, $J_{1,1'}$ = 10.4, $J_{1,2\beta}$ = 7.8 Hz, H1), 1.279 (1 H, dddd, $J_{2\beta,2\alpha}$ = 10.4, $J_{2\beta,1}$ = 7.4, $J_{2\beta,3\alpha}$ = 6.5, $J_{2\beta,3\beta}$ = 5.2 Hz, H2β), 1.31–1.50 (3 H, m, H7α, H2′), 1.53–1.61 (1 H, m, H1′), 1.563 (1 H, dddd, $J_{6\beta,7\alpha}$ = 14.1, $J_{6\beta,6\alpha}$ = 12.6, $J_{6\beta,5}$ = 9.6, $J_{6\beta,7\beta}$ = 2.6 Hz, H6β), 1.69–1.78 (1 H, m, H2α), 1.775 (1 H, br s, $W_{h/2}$ = 7.7 Hz, OH), 1.899 (1 H, ddd, $J_{7\beta,7\alpha}$ = 12.7, $J_{7\beta,6\alpha}$ = 4, $J_{7\beta,6\beta}$ = 2.6 Hz, H7β), 1.923 (1 H, ddddd, $J_{6\alpha,6\beta}$ = 12.6, $J_{6\alpha,5}$ = 6.6, $J_{6\alpha,7\beta}$ = 4, $J_{6\alpha,7\alpha}$ = 2.4, $J_{6\alpha,4}$ = 1 Hz, H3α), 2.047 (1 H, ddddd, $J_{3\alpha,3\beta}$ = 16.6, $J_{3\alpha,2\alpha}$ = 9.8, $J_{3\alpha,2\beta}$ = 6.8, $J_{3\alpha,5}$ = 1.4, $J_{3\alpha,4}$ = 1 Hz, H3α), 2.123 (1 H, dddd, $J_{3',P}$ = 14.6, $J_{3',3'}$ = 14.6, $J_{3',2'}$ = 12.4, $J_{3',2'}$ = 4 Hz, H3′), 2.27–2.35 (1 H, m, H3β), 2.291 (1 H, dddd, $J_{3',P}$ = $J_{3',3'}$ = 14.8, $J_{3',2'}$ = 11.7, $J_{3',2'}$ = 4.6 Hz, H3′), 4.17–4.26 (1 H, m, H5), 5.249 (1 H, dddd, $J_{4,5}$ = 1.2, $J_{4,6\alpha}$ = 1.2, $J_{4,3\beta}$ = 1.2, $J_{4,3\alpha}$ = 1.2 Hz, H4), 7.44–7.55 (6 H, m, C_6H_5 meta, para), 7.71–7.77 (4 H, m, C_6H_5 ortho); preirradiation at δ 4.21 (H5), resulted in enhancements at 5.25 (H4) of 4.4%, 1.92 (H6α) of 3.3%, 1.75 (OH) of 5.5%, and 1.39 (H7α), of 2.8%; preiiradiation at δ 0.93 (7a-CH_3) resulted in enhancements at 2.32 (H3β), 1.90 (H7β), 1.90 (H7β), 1.58 (H2′, H6β), and 1.28 (H2β). Anal. Calcd for $C_{26}H_{33}O_2P$: C, 76.4; H, 8.1. Found: C, 76.1; H, 7.9.

From the Hydrindenone 15. DIBAL-H (2.4 mL, 4.2 mmol, 25% solution in toluene) was added to a stirred of the hydrindenone **15** (706 mg, 1.39 mmol) in dichloromethane (15 mL) at −50 °C to give immediate reduction to the corresponding alcohol. The mixture was worked up as described above to give a clear viscous oil, which was submitted to flash chromatography with 1:49 graded to 1:24 methanol–ethyl acetate. The resulting colorless viscous oil was triturated with ether and dried thoroughly under high vacuum to afford **(1*RS*,1′*RS*,5*SR*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyl-2,3,5,6,7,7a-hexahydro-1*H*-inden-5-ol (17)** as a white brittle foam (530 mg, 75%). ^{1}H NMR: δ 0.908 (3 H, s, 7a-CH_3), 0.959 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.6 Hz, 1′-CH_3), 1.143 (1 H, ddd, $J_{1,2\alpha}$ = 11.5, $J_{1,1'}$ = 9.6, $J_{1,2\beta}$ = 7.3 Hz, H1), 1.29–1.50 (3 H, m, H7α, H2β, H5‴α), 1.582 (1 H, ddqd, $J_{1',1}$ = 9.8, $J_{1',2'}$ = 7.6, $J_{1',1'\text{-Me}}$ = 6.6, $J_{1',2'}$ = 3.0 Hz, H1′), 1.695 (1 H, dddd, $J_{6\beta,7\alpha}$ = 14.1, $J_{6\beta,\alpha}$ = 12.6, $J_{6\beta,5}$ = 9.6, $J_{6\beta,7\beta}$ = 3 Hz, H6β), 1.70–1.83 (2 H, m, H2α, H2′), 1.885 (1 H, ddd, $J_{7\beta,7\alpha}$ = 12.6, $J_{7\beta,6\alpha}$ = 3.6, $J_{7\beta,6\beta}$ = 3.0 Hz, H7β), 1.984 (1 H, dddd, $J_{6\alpha,6\beta}$ = 12.7, $J_{6\alpha,5}$ = 6.6, $J_{6\alpha,7\beta}$ = 3.6, $J_{6\alpha,7\alpha}$ = 0.5 Hz, H6α), 2.091 (1 H, dddd, $J_{3\alpha,3\beta}$ = 12.3, $J_{3\alpha,2\alpha}$ = 7.5, $J_{3\alpha,2\beta}$ = 5.0, $J_{3\alpha,5}$ = 1.0 Hz, H3α), 2.10–2.21 (3 H, m, H2′, H3′, H5‴β), 2.22–2.35 (2 H, m, H3′, H3β), 2.324 (1 H, dd, $J_{1'',1''}$ = 14.6, $J_{1'',2'''}$ = 6.2 Hz, H1″), 2.445 (1 H, ddd, $J_{1'',1''}$ = 14.6, $J_{1'',2'''}$ = 3.8, $J_{1'',3}$ = 0.5 Hz, H1″), 3.69–3.81 (3 H, m, H4‴α, H6‴α, OH), 4.03–4.14 (3 H, m, H4‴β, H6‴β, H5), 4.518 (1 H, dd, $J_{2''',1''}$ = 6.5, $J_{2''',1''}$ = 3.8 Hz, H2‴), 7.44–7.55 (6 H, m, C_6H_5 meta, para), 7.71–7.77 (4 H, m, C_6H_5 ortho). HRMS: calcd for $C_{31}H_{41}O_4P$ 508.2742, found 508.2748.

Workup with dilute acid led to formation of substantial amounts of the less polar diene **18** resulting from dehydration. This was demonstrated by the following experiment. The hydrindenol **17** (81 mg, 0.16 mmol) in THF (5 mL) containing hydrochloric acid (1 M, 10 mL) was stirred for 30 min. The mixture was extractd with ether, and the extracts were washed with brine and dried (Na_2SO_4). The ether was evaporated to leave an oil, which was immediately purified by flash chromatography with ethyl acetate to give an 8:1 mixture of **(1*RS*,1′*RS*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyl-2,6,7,7a-tetrahydro-1*H*-indene (18)** and the corresponding aldehyde as a white foam (57 mg). The diene **18** was unstable and was identified by ^{1}H NMR spectroscopy: δ 0.807 (3 H, s, 7a-CH_3), 0.982 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.6 Hz, 1′-CH_3), 1.311 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.4, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.6, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.3 Hz, H5‴α), 1.390 (1 H, dd, $J_{7\alpha,7\beta}$ = 12.6, $J_{7,6}$ = 5.5 Hz, H7α or H7β), 1.38–1.46 (1 H, m, H2′), 1.536 (1 H, ddd, $J_{1,2\beta}$ = $J_{1,1'}$ = 10.4, $J_{1,2\alpha}$ = 7.6 Hz, H1), 1.752 (1 H, dddq, $J_{1',1}$ = 10.6, $J_{1',2'}$ = 7.9, $J_{1',1'\text{-Me}}$ = 6.6, $J_{1',2'}$ = 3.2 Hz, H1′), 1.75–1.87 (1 H, m, H2′), 1.926 (1 H, br dd, $J_{6\alpha,6\beta}$ = 13.3, $J_{6\alpha,7\beta}$ = 5.1 Hz, H6α), 1.95–2.35 (4 H, m, H7α or H7β, H3′, H2β), 2.062 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.4, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.2, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 4.9 Hz, H5‴α), 2.07–2.15 (1 H, m, H6β), 2.248 (1 H, ddd, $J_{2\alpha,2\beta}$ = 15.9, $J_{2\alpha,1}$ = 7.4, $J_{2\alpha,3}$ = 3 Hz, H2α), 2.365 (1 H, dd, $J_{1''\alpha,1''\beta}$ = 14.3, $J_{1''\alpha,2'''}$ = 5.6 Hz, H1″α), 2.462 (1 H, ddd, $J_{1''\beta,1''\alpha}$ = 14.3, $J_{1''\beta,2'''}$ = 4.3, $J_{1''\beta,5}$ = 1 Hz, H1″β), 3.67–3.79 (2 H, m, H4‴α/H6‴α), 4.06–4.11 (2 H, m, H4‴β/H6‴β), 4.603 (1 H, dd, $J_{2''',1''\alpha}$ = 5.7, $J_{2''',1''\beta}$ = 4.4 Hz, H2‴), 5.414 (1 H, br m, $W_{h/2}$ = 6.5 Hz, H3), 5.581 (1 H, br m, $W_{h/2}$ = 10.2 Hz, H5), 7.45–7.55 (6 H, m, C_6H_5 meta, para), 7.73–7.79 (4 H, m, C_6H_5 ortho).

Horner–Wittig Reaction with the Hydrindenol 17. The hydrindenol **17** (400 mg, 0.80 mmol) in THF (15 mL) was treated with butyllithium at 0 °C until the orange color due to the dianion persisted. Approximately 1 equiv (ca. 0.5 mL) of the butyllithium solution was required; however, a sharp end point indicating onset of formation of the dianion was difficult to obtain. An additional 1 equiv of butyllithium (0.49 mL, 0.84 mmol, 1.7 M in hexane) was then added, to give a bright orange heterogeneous mixture. This was cooled to −75 °C, and then a solution of α-methacrolein

(59 mg, 0.84 mmol) in THF (1 mL) was added dropwise. This operation completely decolorized the mixture. This was allowed to warm to room temperature over 2 h, whereupon saturated ammonium chloride solution (10 mL) was added. The mixture was extracted with ethyl acetate (2 × 50 mL), and the combined extracts were washed with brine and dried (Na_2SO_4). Removal of the solvents by evaporation under reduced pressure gave an almost colorless oil, which contained two major components as shown by TLC analysis. Isolation of these by radial chromatography with 1:49 methanol–ethyl acetate revealed that these were both diastereomeric mixtures of the β-hydroxy phosphine oxide adducts. These were obtained after thorough drying under high vacuum as colorless brittle foams (337 mg, 73% combined). The β-hydroxy phosphine oxide mixture (337 mg, 0.58 mmol) was dissolved in dry DMF (6 mL), and then sodium hydride (84 mg, 1.9 mmol, 55% dispersion in oil) was added all at once. Addition was associated with the formation of a precipitate. The mixture was stirred under nitrogen at 70 °C (bath temperature) for 1 h, during which time it became golden brown. Brine (10 mL) was added, and the product was extracted into ether (3 × 50 mL). The combined extracts were dried (Na_2SO_4). Removal of the solvent under reduced pressure and the residual DMF under high vacuum left an orange oil (252 mg). This was submitted to flash chromatography with 1:1 ether–petroleum ether to give a 71:29 mixture of *E* and *Z* isomers of **(1*RS*,1′*RS*,5*SR*,7a*RS*)-1-(1′,5′-dimethylhexa-3′,5′-dienyl)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-7a-methyl-2,3,5,6,7,7a-hexahydro-1*H*-inden-5-ol (19)** as an unstable colorless viscous oil (91 mg, 31% from the hydrindenol). ^1H NMR [(*) denotes the *Z* isomer]: δ 0.948, 0.957* (3 H, d, $J_{1'\text{-Me},1'}$ = 6.7 Hz, 1′-CH_3), 0.966*, 0.969 (3 H, s, 7a-CH_3), 1.178 (1 H, ddd, $J_{1,2\alpha}$ = 11.5, $J_{1,1'}$ = 9.9, $J_{1,2\beta}$ = 7.4 Hz, H1), 1.31–1.52 (3 H, m, H2β, H5‴α, H7α), 1.53–1.63 (1 H, m, H1′), 1.66–2.03 (5 H, m, H2α, H3β, H6, H7β), 1.838 (3 H, t, $J_{5'\text{-Me},6'E}$ = 1.2, $J_{5'\text{-Me},6'Z}$ = 1.2 Hz, 5′-CH_3), 1.866* (3 H, dd, $J_{5'\text{-Me},6'Z}$ = 1.5, $J_{5'\text{-Me},6'E}$ = 1 Hz, 5′-CH_3), 2.05–2.31 (4 H, m, H2′, H3α, H5‴β), 2.343, 2.349* (1 H, dd, $J_{1''\alpha,1''\beta}$ = 14.3, $J_{1''\beta,2'''}$ = 6.4 Hz, H1″α), 2.468*, 2.470 (1 H, ddd, $J_{1''\beta,1''\alpha}$ = 14.3, $J_{1''\beta,2'''}$ = 3.8, $J_{1''\beta,3}$ = 0.7 Hz, H1″β), 3.68–3.83 (3 H, m, H4‴α, H6‴α, OH), 4.05–4.17 (3 H, m, H4‴β, H5, H6‴β), 4.535*, 4.542 (1 H, dd, $J_{2'''1''\alpha}$ = 6.4, $J_{2'''1''\beta}$ = 3.8 Hz, H2‴), 4.825* (1 H, br m, $W_{h/2}$ = 4.8 Hz, H6′*E*), 4.862 (2 H, s, H6′), 4.938* (1 H, br m, $W_{h/2}$ = 5.5 Hz, H6′*Z*), 5.411* (1 H, ddd, $J_{3',4'}$ = 11.8, $J_{3',2'}$ = 8.5, $J_{3',2'}$ = 6.1 Hz, H3′), 5.624 (1 H, ddd, $J_{3',4'}$ = 15.5, $J_{3',2'}$ = 8.3, $J_{3',2'}$ = 6.5 Hz, H3′), 5.889* (1 H, br dm, $J_{4',3'}$ = 11.8, $W_{h/2}$ = 4.4 Hz, H4′), 6.131 (1 H, d, $J_{4',3'}$ = 15.6 Hz, H4′). HRMS: calcd for $C_{23}H_{36}O_3$ 360.2664, found 360.2666.

Preparation of Hydrindanones. A solution of the hydrindenone **15** (1.898 g, 3.75 mmol) in ethanol (30 mL) containing pyridine (10 drops, ca. 0.05 mL) was shaken with 10% palladium on charcoal (190 mg) under a hydrogen atmosphere at 820 psi (56 atm) for 22 h. Removal of the catalyst by filtration followed by evaporation of the solvent left a viscous oil, a ^1H NMR spectroscopic examination of which showed that it contained the hydrindanones **20** and **21** in a ratio of 75:25. The mixture was dissolved in methanol (5.4 mL) containing sodium methoxide (0.6 mL, 1 M solution in methanol), and the resulting solution was heated under reflux with stirring for 2 h, during which time it became yellow-orange in color. Aqueous ammonium chloride solution (1 mL) was added, thereby causing decolorization to occur. The methanol was removed by evaporation under reduced pressure. Extraction with ether–dichloromethane (2:1) followed by the usual workup gave an oil, which was submitted to radial chromatography with ethyl acetate and then 1:49 methanol–ethyl acetate to give **(1*RS*,1′*RS*,3a*SR*,4*SR*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyloctahydro-5*H*-inden-5-one (20)** and the *cis*-hydrindanone **22** in a ratio of 95:5 as a white powder (1.598 g, 84% overall). The hydrindanone **20** crystallized from ethyl acetate as a fine microcrystalline powder, mp 151–154 °C. ^1H NMR: δ 0.949 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.6 Hz, 1′-CH_3), 0.960 (3 H, s, 7a-CH_3), 1.155 (1 H, ddd, $J_{1,1'} = J_{1,2\alpha} = J_{1,2\beta}$ = 9.1 Hz, H1), 1.23–1.41 (3 H, m, H2, H2′, H3), 1.304 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.5, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.6, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.3 Hz, H5‴α), 1.418 (1 H, ddd, $J_{1''\beta,1''\alpha}$ = 13.9, $J_{1''\beta,2'''}$ = 8.0, $J_{1''\beta,4}$ = 2.8 Hz), 1.46–1.65 (4 H, m, H1′, H3, H3a, H7), 1.70–1.85 (2 H, m, H2, H2′), 1.887 (1 H, ddd, $J_{1''\alpha,1''\beta}$ = 13.8, $J_{1''\alpha,4}$ = 9.7, $J_{1''\alpha,2'''}$ = 3.3 Hz, H5‴β), 2.05–2.17 (2 H, m, H3′, H7), 2.21–2,23 (2 H, m, H3′, H6β), 2.474 (1 H, dd, $J_{6\alpha,6\beta}$ = 14.4, $J_{6\alpha,7\alpha}$ = 6.6 Hz, H6α), 2.542 (1 H, dddd, $J_{4,3a}$ = 12.7, $J_{4,1''\alpha}$ = 9.7, $J_{4,1''\beta}$ = 2.9, $J_{4,6\beta}$ < 0.5 Hz, H4), 3.64–3.81 (2 H, m, H4‴α, H6‴α), 4.01–4.09 (2 H, m, H4‴β, H6‴β), 4.747 (1 H, dd, $J_{2'''1''\beta}$ = 7.9, $J_{2'''1''\alpha}$ = 3.2 Hz, H2‴), 7.44–7.55 (6 H, m, C_6H_5 meta, para), 7.71–7.78 (4 H, m, C_6H_5 ortho). Anal. Calcd for $C_{31}H_{41}O_4P$: C, 73.2; H, 8.1. Found: C, 73.0; H, 8.2.

Preparation of Hydrindanol 23. A solution of the hydrindanone **20** (366 mg, 0.72 mmol) in dichloromethane (15 mL) was treated dropwise with DIBAL-H (1.5 mL, 2.2 mmol, 20% solution in hexane) at −70 °C. TLC analysis indicated that the reaction took place immediately. The reaction mixture was warmed to 0 °C during 30 min, and then saturated sodium sulfate solution (5 mL) was added. Stirring was continued at room temperature until solid material had precipitated out (30 min). This was removed by filtration. The filtrate was dried (Na_2SO_4) and evaporated under reduced pressure to leave a viscous oil, which was submitted to flash chromatography with 1:49 methanol–ethyl acetate to give a 79:21 mixture of the β- and α-epimers of **(1*RS*,1′*RS*,3a*SR*,4*SR*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyloctahydro-1*H*-inden-5-ol (23)** as a white brittle foam (329 mg, 79%). Attempts to separate the epimers by HPLC were unsuccessful. ^1H NMR [(*) denotes the α-epimer]: δ 0.637*, 0.713 (3 H, s, 7a-CH_3), 0.931, 0.940* (3 H, d, $J_{1'\text{-Me},1'}$ = 6.5 Hz, 1′-CH_3), 1.02–1.23 (4 H, m, H1, H2β, H3α, H7α), 1.343 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.6, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.5, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.2 Hz, H5‴α), 1.34–1.89 (12 H, m, H1′, H1″, H2α, H2′, H3β, H3, H4, H6, H7β), 2.02–2.17 (2 H, m, H3′, H5‴β), 2.291 (1 H, dddd, $J_{3',P}$ = 14.6, $J_{3',3'}$ = 12.8, $J_{3',2'}$ = 11.9, $J_{3',2'}$ = 4.4 Hz, H3′), 3.227 (1 H, ddd, $J_{5,4or6\beta}$ = 10.9, $J_{5,4or6\beta}$ = 8.9, $J_{5,6\alpha}$ = 5.4 Hz, H5), 3.72–3.82 (2 H, m, H4‴α, H6‴α), 3.935* (1 H, br m, $W_{h/2}$ = 7.0 Hz, H5), 4.001 (1 H, br m, $W_{h/2}$ = 13.3 Hz, OH), 4.07–4.15 (2 H, m, H4‴β, H6‴β), 4.656 (1 H, dd, $J_{2'''1''}$ = 5.1, $J_{2'''1''}$ = 3.8 Hz, H2‴), 7.43–7.56 (6 H, m, C_6H_5 meta, para), 7.68–7.80 (4 H, m, C_6H_5 ortho). Anal. Calcd for $C_{31}H_{43}O_4P$: C, 72.9; H, 8.5. Found: C, 72.7; H, 8.5.

Preparation of Methyl Ether 24. The hydrindanol **23** (298 mg, 0.58 mmol) in THF (5 mL) was added to a stirred suspension of sodium hydride (17 mg, 0.70 mmol) in THF (5 mL) under nitrogen. The resulting mixture was stirred under reflux for 30 min and allowed to cool, and then methyl iodide (40 μL, 0.64 mmol) was added. Stirring was continued at room temperature for 26 h. Saturated ammonium chloride solution (10 mL) was added, and the mixture was extracted with ether–dichloromethane (2:1, 2 × 75 mL). The combined extracts were washed with brine (10 mL) and dried (Na_2SO_4). Evaporation of the solvent left a viscous oil, which was submitted to radial chromatography with 1:49 methanol–ethyl acetate. This gave a 9:1 mixture of β- and α-epimers of the methyl ether **24** as a white brittle foam (153 mg, 50%). Also recovered was the hydrindanol **23** (78 mg, 26%) as a 53:47 mixture of β- and α-epimers. **(1*RS*,1′*RS*,3a*SR*,4*SR*,5*SR*,7a*RS*)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-1-[3′-(diphenylphosphinoyl)-1′-methylpropyl]-7a-methyloctahydro-1*H*-inden-5-ol methyl ether (24)** was isolated by radial chromatography. ^1H NMR: δ 0.689 (3 H, s, 7a-CH_3), 0.928 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.7 Hz, 1′-CH_3), 1.00–1.23 (4 H, m, H1, H2β, H3α, H7α), 1.30 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.6, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.6, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.4 Hz, H5‴α), 1.33–1.49 (3 H, m, H2′, H4, H6β), 1.477 (1 H, dddq, $J_{1',9}$ = 10.4, $J_{1',2'}$ = 7.8, $J_{1',1'\text{-Me}}$ = 6.7, $J_{1',2'}$ = 2.9 Hz, H1′), 1.54–1.64 (4 H, m, H1″, H3a, H3β), 1.67–1.79 (2 H, m, H2α, H2′), 1.82–1.97 (2 H, m, H6α, H7β), 2.058 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.4, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.6, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 5.0 Hz, H5‴β), 2.102 (1 H, dddd, $J_{3',P}$ = 15, $J_{3',3'}$ = 12.2, $J_{3',2'}$ = 12.2, $J_{3',2'}$ = 4.2 Hz, H3′), 2.293 (1 H, dddd, $J_{3',P}$ = 14.7, $J_{3',3'}$ = 12.6, $J_{3',2'}$ = 11.5, $J_{3',2'}$ = 4.5 Hz, H3′), 2.773 (1 H, ddd, $J_{5,4or6\beta}$ = 11.3, $J_{5,4or6\beta}$ = 9.5, $J_{5,6\alpha}$ = 5.0 Hz, H5), 3.327 (3 H, s, CH_3O), 3.70–3.78 (2 H, m, H4‴α, H6‴α), 4.05–4.11 (2 H, m, H4‴β, H6‴β), 4.690 (1 H, t, $J_{2'''1''}$ = 5.5 Hz, H2‴), 7.31–7.54 (6 H, m, C_6H_5 meta, para), 7.71–7.77 (4 H, m, C_6H_5 ortho). Anal. Calcd for $C_{32}H_{45}O_4P$: C, 73.3; H, 8.65. Found: C, 73.7; H, 9.0.

Horner–Wittig Reaction with the Hydrindanol 23. The hydrinanol **23** (470 mg, 0.92 mmol) in THF (40 mL) at −10 °C was treated with a solution of LDA (0.63 M in THF, ca. 1.5 mL or 1 equiv) until the orange color due to the dianion persisted for a couple of minutes before fading. This was taken as the apparent end point; a further 2 equiv of LDA (2.92 mL, 1.84 mmol, 0.63 M in THF) was added to give an intensely orange colored

heterogeneous mixture. This was stirred at −10 °C for 20 min and then cooled to −90 °C. α-Methacrolein (152 μL, 1.40 mmol) was added dropwise to give a pale yellow mixture, which was then allowed to warm to 0 °C over 25 min, during which time it became colorless. Brine (10 mL) was added, and the whole was shaken with ether–dichloromethane (2:1, 150 mL). The organic layer was separated, dried (Na_2SO_4), and evaporated under reduced pressure to leave a viscous oil, which was mainly a mixture of diastereomers of the β-hydroxy phosphine oxide **25**. The oil was submitted to flash chromatography with 1:99 methanol–ethyl acetate and then radial chromatography with ethyl acetate graded to 5:19 methanol–ethyl acetate to give the product as a colorless foam (376 mg, 70%) and unreacted hydrindanol **23** (81 mg, 17%). The product mixture (376 mg, 0.65 mmol) in DMF (4 mL) was added to a suspension of sodium hydride (85 mg, 1.9 mmol, 55% dispersion in oil, washed with pentane prior to use) in DMF (5 mL) with stirring. The resulting mixture was then heated at 70 °C (bath) for 1 h, during which time it became golden brown in color and formation of a precipitate took place. Water (10 mL) was added followed by ether–dichloromethane (2:1, 75 mL). The whole was shaken, and then the organic layer was separated, washed with brine, and dried (Na_2SO_4). Evaporation of the solvents under reduced pressure left an orange oil containing the diene **26** and the hydrindanol **23** in an approximately equimolar ratio. Separation of the products by flash chromatography with 1:49 methanol–ethyl acetate gave the diene as an unstable colorless viscous oil (110 mg, 47% from the β-hydroxy phosphine oxide **25** or 40% overall based on reacting hydrindanol **23**] and the hydrindanol **23** as a brittle foam (125 mg, 38% from the hydroxy phosphine oxide **25** or 32% overall recovery based on reacting hydrindanol **23**). The diene **26** was a mixture of α- and β-epimers, which were separated by flash chromatography. These were both 74:26 mixtures of *E* and *Z* isomers at C5′ and were identified by NMR spectroscopy. The first to be eluted was the α-epimer, **(1*RS*,1′*RS*,3a*SR*,4*SR*,5*RS*,7a*RS*)-1-(1′,5′-dimethylhexa-3′,5′-dienyl)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-7a-methyloctahydro-1*H*-inden-5-ol.** ^1H NMR [(*) denotes the *Z* isomer]: δ 0.687 (3 H, s, 7a-CH_3), 0.929, 0.939* (3 H, d, $J_{1'\text{-Me},1'}$ = 6.7 Hz, 1′-CH_3), 1.02–1.13 (1 H, m, H1), 1.17–1.31 (2 H, m), 1.43–1.75 (11 H, m, H1′, H1″, H2, H3a, H4, H6, H7), 1.348 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.5, $J_{5'''\alpha,4'''\alpha,4'''\alpha/6'''\alpha}$ = 2.7, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.4 Hz, H5‴α), 1.80–1.90 (1 H, m, H2′), 1.832 (3 H, dd, $J_{5'\text{-Me},6'}$ = 1.3, $J_{5'\text{-Me},6'}$ = 0.9 Hz, 5′-CH_3), 2.086 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.4, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.6, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 4.8 Hz, H5‴β), 2.17–2.24 (1 H, m, H2′), 2.26–2.34* (1 H, m, H2′), 2.468*, 2.489 (1 H, d, $J_{OH,5}$ = 3.9 Hz, OH), 3.73–3.81 (2 H, m, H4‴α, H6‴α), 4.08–4.14 (2 H, m, H4‴β, H6‴β), 3.949 (1 H, br m, $W_{h/2}$ = 8.0 Hz, H5), 4.660 (1 H, t, $J_{2''',1''}$ = 4.5 Hz, H2‴), 4.821* (1 H, br m, $W_{h/2}$ = 5 Hz, H6′Z), 4.852 (2 H, br m, $W_{h/2}$ = 2.8 Hz, H6′), 4.924* (1 H, br m, $W_{h/2}$ = 5 Hz, H6′E), 5.399* (1 H, ddd, $J_{3',4'}$ = 11.8, $J_{3',2'}$ = 8.4, $J_{3',2'}$ = 6.1 Hz, H3′), 5.620 (1 H, ddd, $J_{3',4'}$ = 15.3, $J_{3',2'}$ = 8.2, $J_{3',2'}$ = 6.4 Hz, H3′), 5.874* (1 H, d, $J_{4',3'}$ = 11.9 Hz, H4′), 6.114 (1 H, d, $J_{4',3'}$ = 15.2 Hz, H4′).

This was followed by the β-epimer, **(1*RS*,1′*RS*,3a*SR*,4*SR*,5*SR*,7a*RS*)-1-(1′,5′-dimethylhexa-3′,5′-dienyl)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-7a-methyloctahydro-1*H*-inden-5-ol (26a).** ^1H NMR [(*) denotes the *Z* isomer]: δ 0.798 (3 H, s, 7a-CH_3), 0.954, 0.963* (3 H, d, $J_{1'\text{-Me},1'}$ = 6.7 Hz, 1′-CH_3), 1.11–1.42 (4 H, m), 1.47–1.69 (5 H, m), 1.75–1.99 (6 H, m), (H1, H1′, H1″, H2, H2′, H3, H3a, H4, H6, H7), 1.386 (1 H, dtt, $J_{5'''\alpha,5'''\beta}$ = 13.5, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.5, $J_{5'''4'''\beta/6'''\beta}$ = 1.2 Hz, H5‴α), 1.869 (3 H, dd, $J_{5'\text{-Me},6'}$ = 1.3, $J_{5'\text{-Me},6'}$ = 0.9 Hz, 5′-CH_3), 2.129 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.5, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.8, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 4.8 Hz, H5‴β), 2.21–2.28 (1 H, m, H2′), 2.29–2.37* (1 H, m, H2′), 3.284 (1 H, dddd, $J_{5,4}$ = 9.0, $J_{5,6\beta}$ = 9.0, $J_{5,6\alpha}$ = 5.1, $J_{5,OH}$ = 2.4 Hz, H5), 3.78–3.87 (2 H, m, H4‴α, H6‴α), 4.027, 4.057* (1 H, Hz, H4′). $J_{OH,5}$ = 2.5 Hz, OH), 4.12–4.69 (2 H, m, H4‴β, H6‴β), 4.714 (1 H, dd, $J_{2''',1''}$ = 5.1, $J_{2''',1''}$ = 3.9 Hz, H2‴), 4.852* (1 H, br s, $W_{h/2}$ = 4.9 Hz, H6′Z, 4.960* (1 H, br s, $W_{h/2}$ = 4.9 Hz, H6′E), 4.888 (2 H, br s, $W_{h/2}$ = 2.8 Hz, H6′), 5.427* (1 H, ddd, $J_{3',4'}$ = 11.7, $J_{3',2'}$ = 8.8, $J_{3',2'}$ = 6.2 Hz, H3′), 5.649 (1 H, ddd, $J_{3',4'}$ = 15.2, $J_{3',2'}$ = 8.5, $J_{3',2'}$ = 6.2 Hz, H3′), 5.912* (1 H, d, $J_{4',3'}$ = 11.9 Hz, H4′), 6.145 (1 H, d, $J_{4',3'}$ = 15.2 Hz, H4′).

Hydrogenation of the Diene 26a. The β-epimer **26a** of the diene **26** (71 mg, 0.20 mmol) in ethanol (5 mL) was stirred under a hydrogen atmosphere (1 atm) in the presence of 10% palladium on charcoal (7 mg) for 1 h. The catalyst was removed by filtration, and the filtrate was evaporated to dryness, leaving the saturated product as a viscous oil. This was purified by flash chromatography (ether–petroleum ether, 1:1) to give **(1*RS*,1′*RS*,3a*SR*,4*SR*,5*SR*,7a*SR*)-1-(1′,5′-dimethylhexyl)-4-[(1‴,3‴-dioxan-2‴-yl)methyl]-7a-methyloctahydro-1*H*-inden-5-ol (27)** as a colorless viscous oil (69 mg, 97%). ^1H NMR: δ 0.750 (3 H, s, 7a-CH_3), 0.858 (3 H, d, $J_{5'\text{-Me},5'}$ = 6.6 Hz, 5′-CH_3), 0.863 (3 H, d, $J_{6',5'}$ = 6.6 Hz, H6′), 0.899 (3 H, d, $J_{1'\text{-Me},1'}$ = 6.6 Hz, 1′-CH_3), 1.06–1.41 (10 H, m), 1.48–1.63 (4 H, m), 1.80–1.94 (3 H, m), (H1, H1′, H2, H2′, H3, H3′, H3a, H4, H4′, H5′, H7), 1.353 (1 H, dt, $J_{5'''\alpha,5'''\beta}$ = 13.7, $J_{5'''\alpha,4'''\alpha/6'''\alpha}$ = 2.6, $J_{5'''\alpha,4'''\beta/6'''\beta}$ = 1.3 Hz, H5‴α), 1.532 (1 H, ddd, $J_{1''\beta,1''\alpha}$ = 14.2, $J_{1''\beta,4}$ = 8.0, $J_{1''\beta,2'''}$ = 5.4 Hz, H1″β), 1.586 (1 H, dddd, $J_{6\beta,6\alpha}$ = 13.6, $J_{6\beta,5or7\alpha}$ = 13.6, $J_{6\beta,5or7\alpha}$ = 11.3, $J_{6\beta,7\beta}$ = 4.4 Hz, H6β), 1.800 (1 H, dddd, $J_{6\alpha,6\beta}$ = 13.4, $J_{6\alpha,5or7\alpha}$ = 5.3, $J_{6\alpha,5or7\alpha}$ = 4.1, $J_{6\alpha,7\beta}$ = 2.9 Hz, H6α), 1.851 (1 H, ddd, $J_{1''\alpha,1''\beta}$ = 14.2, $J_{1''\alpha,2'''}$ = 3.8, $J_{1''\alpha,4}$ = 1.9 Hz, H1″α), 2.098 (1 H, dtt, $J_{5'''\beta,5'''\alpha}$ = 13.7, $J_{5'''\beta,4'''\alpha/6'''\alpha}$ = 12.6, $J_{5'''\beta,4'''\beta/6'''\beta}$ = 5.0 Hz, H5‴β), 3.21–3.29 (1 H, m, H5), 3.75–3.83 (2 H, m, H4‴α, H6‴α), 3.990 (1 H, br s, $W_{h/2}$ = 5.2 Hz, OH), 4.09–4.17 (2 H, m, H4‴β, H6‴β), 4.676 (1 H, dd, $J_{2''',1''\beta}$ = 5.1, $J_{2''',1''\alpha}$ = 4.0 Hz, H2‴). HRMS: calcd for $C_{23}H_{42}O_3$ 366.3133, found 366.3136. Anal. Calcd for $C_{23}H_{42}O_3$: C, 75.4; H, 11.6. Found: C, 75.7; H, 11.3.

Registry No. **2**, 1120-73-6; **3**, 17668-60-9; **4**, 21860-46-8; **5**, 108643-98-7; **6**, 108662-09-5; **7**, 120454-08-2; **9** (isomer 1), 122406-49-9; **9** (isomer 2), 122406-50-2; **10**, 122406-51-3; **11**, 122406-52-4; **12**, 122334-18-3; **13**, 122334-19-4; **14**, 122334-20-7; **15**, 122334-21-8; **16**, 122334-22-9; **17**, 122334-23-0; **17** β-hydroxy phosphine oxide deriv (isomer 1), 122334-24-1; **17** β-hydroxy phosphine oxide deriv (isomer 2), 122406-53-5; **17** β-hydroxy phosphine oxide deriv (isomer 3), 122406-54-6; **17** β-hydroxy phosphine oxide deriv (isomer 4), 122406-55-7; **18**, 122334-25-2; **19** (isomer 1), 122334-26-3; **19** (isomer 2), 122406-56-8; **20**, 122334-27-4; **21**, 122334-28-5; **22**, 122406-57-9; **23** (isomer 1), 122334-29-6; **23** (isomer 2), 122334-30-9; **24** (isomer 1), 122334-31-0; **24** (isomer 2), 122334-32-1; **25**, 122357-49-7; α-(*E*-**26**, 122334-33-2; α-(*Z*)-**26**, 122406-58-0; β-(*E*)-**26**, 122406-59-1; β-(*Z*)-**26**, 122406-60-4; **27**, 122334-34-3; α-methacrolein, 78-85-3; vitamin D, 1406-16-2.

Supplementary Material Available: IR and mass spectral data for compounds **9–13**, **15–17**, **19**, **20**, **23**, **24**, and **27**, 400-MHz ^1H NMR spectra for compounds **9–15**, **17–19**, and **26**, and crystallographic data for compound **15**, including an ORTEP plot and tables of positional parameters, bond lengths and angles, thermal parameters, and hydrogen atom positional and thermal parameters (54 pages). Ordering information is given on any current masthead page.