

Transition-metal-catalysed Grignard Reaction of Secondary Allylic Phosphates

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Regio- and stereo-chemistry of transition-metal-catalysed Grignard reactions of secondary allylic phosphates have been investigated. Best results for regioselective carbon-carbon bond formation at the γ -position of secondary allylic phosphates were attained when copper(I) iodide was used as the catalyst. The naturally occurring monoterpene alcohols, geraniol and the sex pheromone of the African Monarch, were synthesized as a demonstration of the synthetic utility of the newly developed coupling reaction.

There has been increasing interest in developing methods which lead to selective carbon-carbon bond formation at either the α - or γ -position of an allylic system.¹ For such regioselective bond formation, the most straightforward method is the cross-coupling of allylic species and organometallics. Although a variety of organometallic compounds containing various metals such as Li, Mg, Cu, Pd, etc., have been widely examined,^{1,2} allylic substrates which have been hitherto utilized are mainly allylic halides, acetates, and ethers, and the use of allylic phosphates has received relatively little attention.³ Grignard reaction of phosphate esters was first described in the 1920's,⁴ whereas the reaction of allylic phosphates with Grignard reagents was not reported until 1969. Wood and co-workers have synthesized a series of primary allylic diphenyl phosphates⁵ and examined their reactions with Grignard reagents.⁶ They have described how Grignard reagents regioselectively attack the α -carbon of the phosphates, but the coupling lacks stereoselectivity, i.e., starting with an *E*-allylic diphenyl phosphate, the coupled olefin was a mixture of the *E*- and *Z*-stereoisomers.

Bourgain-Commerçon *et al.* have reported⁷ that copper(I)-catalysed Grignard reaction of primary allylic phosphates readily produce, regioselectively, the α -coupling products. Recently we have found⁸ that geranyl and neryl diethyl phosphates allylate a variety of Grignard reagents regio-specifically at the α -position with preservation of stereo-chemistry.

In order to examine further the scope of the Grignard coupling of allylic phosphates, we have now investigated the Grignard reaction of secondary allylic phosphates in the presence or absence of transition metal catalysts in an attempt to define the regio- and stereo-chemistry of this coupling. Furthermore, its synthetic applications to naturally occurring isoprenoids are also described.

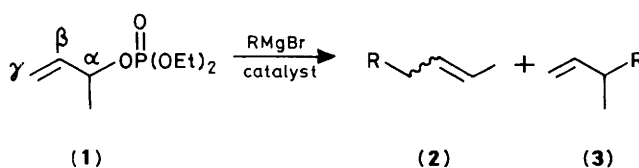
Results and Discussion

Using diethyl 1-methylprop-2-enyl phosphate (1) as a representative secondary allylic phosphate, reaction with phenylmagnesium bromide was examined. The coupling was carried out in diethyl ether at room temperature using an excess (1.7 equiv.) of the Grignard reagent. The products were, after hydrolysis, extracted with diethyl ether and analysed by gas chromatography. Results are summarized in the Table. In the absence of catalysts, an almost 1:1 mixture of the γ - (2; R = Ph) and α -coupling products (3; R = Ph) was formed (Scheme 1). Structures of products (2) and (3) were deduced from spectroscopic data of the pure samples separated by preparative g.l.c. When the reaction was conducted in tetrahydrofuran (THF), the γ : α ratio changed from 52:48 to 82:18. It is worthwhile to note that the *E*:*Z* ratio of the γ -coupling product

Table. Transition-metal-catalysed Grignard reaction of diethyl 1-methylprop-2-enyl phosphate (1)^a

R	Catalyst (mol%) ^b	Solvent	Yield/(%)	Product ratio ^c (2) (<i>E</i> : <i>Z</i>):(3)
Ph	None	Et ₂ O	81	52 (81:19):48
Ph	CuI (10)	Et ₂ O	96	90 (68:32):10
Ph	Li ₂ CuCl ₄ (0.4)	Et ₂ O	97	77 (43:57):23
Ph	Pd(PPh ₃) ₄ (2)	Et ₂ O	80	73 (51:49):27
Ph	Ni(PPh ₃) ₂ Cl ₂ (2)	Et ₂ O	73	63 (79:21):37
Ph	None	THF	82	82 (39:61):18
Ph	CuI (10)	THF	87	86 (50:50):14
Ph	Pd(PPh ₃) ₄ (2)	THF	78	82 (44:56):18
Ph	Ni(PPh ₃) ₂ Cl ₂ (2)	THF	56	78 (50:50):22
Ph	Cp ₂ TiCl ₂ ^d (2)	THF	75	78 (40:60):22
hexyl	None	Et ₂ O	79	40 (50:50):60
hexyl	CuI (10)	Et ₂ O	91	94 (48:52):6
hexyl	Pd(PPh ₃) ₄ (2)	Et ₂ O	77	80 (57:43):20

^a All the reactions were carried out at room temperature using (1) 3 mmol and 5 mmol of the Grignard reagent. ^b Of the Grignard reagent used. ^c Determined by g.l.c. using an Apiezon grease L column (2 m, 120 °C). ^d Cp = cyclopentadienyl.

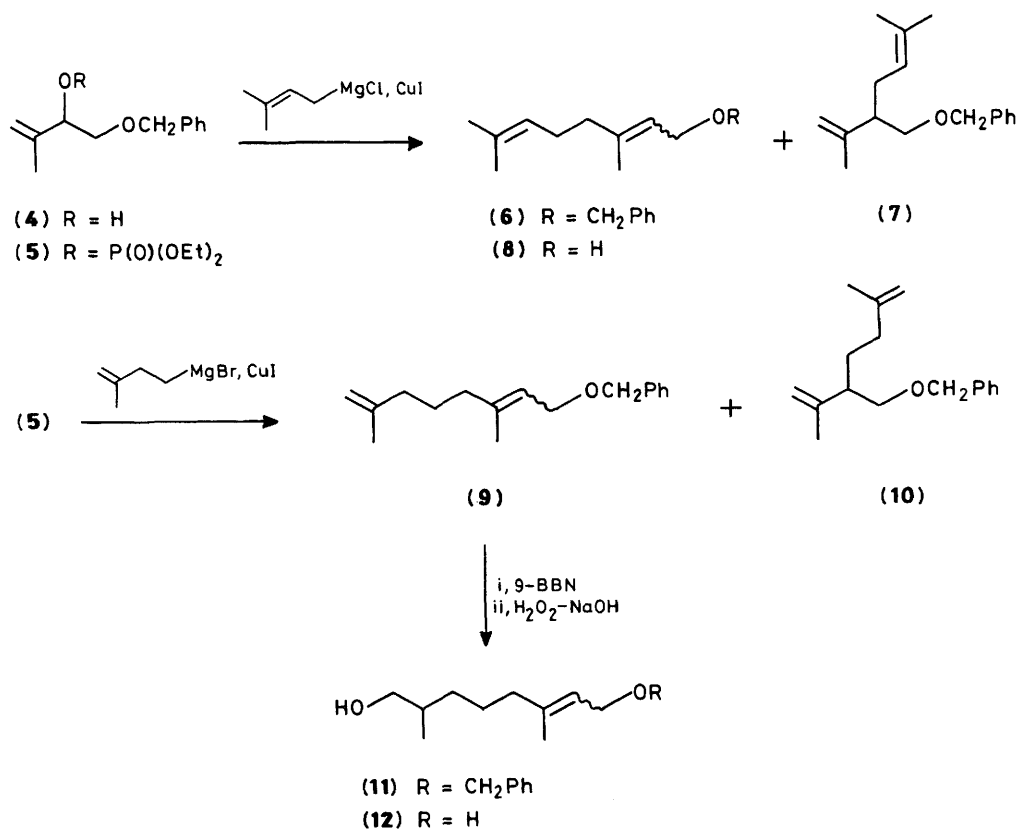


Scheme 1.

(2; R = Ph) produced in diethyl ether is 81:19, while in THF the stereoselectivity was reversed (*E*:*Z* 39:61).

By the addition of transition-metal catalysts, the regio-selectivity (preference for γ -selectivity) was found to increase. Of the five transition-metal catalysts which were examined, copper(I) iodide was the most effective. That is, the highest γ -selectivity (γ : α 90:10) was attained when the coupling was undertaken with 10 mol % of copper(I) iodide, though the stereoselectivity was still unsatisfactory (*E*:*Z* 68:32). The catalytic activity largely depends on the solvent used. In THF, the addition of the catalysts did not essentially change either the regio- or the stereo-selectivity.

The coupling reaction of (1) with hexylmagnesium bromide in diethyl ether was also catalysed by copper(I) iodide. The γ : α ratio (40:60) for the non-catalytic reaction increased to 94:6 by the addition of 10 mol % of copper(I) iodide. Again, the *E*:*Z* ratio of the γ -coupling product (2; R = hexyl) was not improved even in the catalytic reaction.



Scheme 2.

Synthetic Application

In order to illustrate the synthetic utility of the present copper(I)-catalysed Grignard coupling of secondary allylic phosphates, the naturally occurring isoprenoid alcohols (8) and (12) were synthesized from a readily accessible allylic phosphate (5) as shown in Scheme 2. The phosphate (5) was obtained in 71% yield by the phosphorylation of the allylic alcohol (4), which was synthesized in high yield from prenol (3-methylbut-2-en-1-ol) according to the literature method.⁹ The Grignard reaction of (5) and 3-methylbut-2-enylmagnesium chloride was conducted in diethyl ether in the presence of 10 mol % of copper(I) iodide. The coupling proceeded easily to give a mixture of the γ - (6) and the α -coupling product (7) in 88% combined yield. Gas chromatographic analysis revealed that the γ : α ratio was 84:16 and the *E*:*Z* ratio of (6) was 78:22. Pure samples of (6) and (7) were isolated by preparative g.l.c. and the structures were fully characterized by spectral and analytical data. It must be noted that the obtained products (6) and (7) were those coupled at the α -position of the allylic Grignard reagent.¹⁰ No trace of the products coupled at the γ -position of the Grignard reagent could be found. When the same coupling was carried out in THF in the presence of copper(I) iodide, (6) and (7) were formed in the ratio 97 (*E*:*Z* 83:17):3 in 51% yield. Treatment of the mixture of (6) and (7) (from the reaction in THF) with lithium metal in ethylamine followed by column chromatography on silica gel gave geraniol (8) (*E*:*Z* 83:17) in 81% isolated yield.

Further application is shown in the synthesis of the sex pheromone (12) of the male butterflies of the African Monarch (*Danaus chrysippus*).¹¹ Copper(I)-catalysed reaction of 3-methylbut-3-enylmagnesium bromide and (5) in diethyl ether gave a mixture of (9) and (10) [(9):(10) 95:5] in 91% yield. The *E*:*Z* ratio of (9) was 61:39. Analytical and spectroscopic data of (9) and (10) were consistent with the assigned structures. When

THF was used as solvent, the combined yield of (9) and (10) was 91% and the ratio (9):(10) was 94 (*E*:*Z* 77:23):6. In order to introduce a hydroxy group regioselectively to the terminal position of (9), the mixture of (9) and (10) from the reaction in THF was treated with 9-borabicyclo[3.3.1]nonane and then oxidized with an alkaline solution of hydrogen peroxide. Column chromatographic separation of the reaction mixture on silica gel afforded the desired alcohol (11) with preservation of the stereochemistry (*E*:*Z* 79:21) in 86% yield. Debenzylation of (11) with lithium in ethylamine furnished the diol (12) (*E*:*Z* 76:24) in 75% yield. The spectroscopic data of the synthesized pheromone were in complete accord with those of the natural one.¹¹

The above examples show that the present copper(I)-catalysed Grignard reaction of secondary allylic phosphates provides a useful method for the regioselective carbon-carbon bond formation at the γ -position of a secondary allylic system. Furthermore, it is demonstrated that the phosphate (5) is a useful five-carbon synthon for isoprene homologation and can serve as a versatile reagent in the total synthesis of terpenoid compounds.

Experimental

I.r. spectra were recorded on a JASCO IRA-1 spectrophotometer. ¹H N.m.r. spectra were recorded on a Hitachi R-24A spectrometer (60 MHz) with Me₄Si as internal standard. Mass spectra were determined using a Hitachi M-52 instrument at 20 eV. G.l.c. analyses and preparative g.l.c. were performed on a Yanaco G 1800 gas chromatograph. The g.l.c. columns used were 15% Apiezon grease L on Uniport B (1 m or 2 m \times 3 mm), 20% polyethylene glycol (PEG) 20 M on Celite 545 (1 m \times 3 mm), and 10% Silicone SE-30 on Chromosorb W AW (1 m \times 3

mm). Elemental analyses were performed at the Elemental Analysis Centre of Kyoto University. For Kugelrohr distillation, a Shibata GTO-250R glass tube oven was used.

Diethyl 1-Methylprop-2-enyl Phosphate (1).—This phosphate was synthesized by the method of Miller and Wood.⁵ To a solution of 1-methylprop-2-enol (5.3 g, 73 mmol) in pyridine (15 ml) was added diethyl phosphorochloridate (12.7 g, 73 mmol) at 0 °C. The mixture was stirred at 0 °C for 3 h and then poured into sulphuric acid (1M; 200 ml). The product was extracted with diethyl ether and the extracts were washed with saturated aqueous sodium hydrogen carbonate, dried over anhydrous sodium sulphate, and evaporated. The residue was distilled to give compound (1) as an oil (11.5 g, 75%), b.p. 77–79 °C/4 mmHg (Found: C, 45.95; H, 8.45. C₈H₁₇O₄P requires C, 46.15; H, 8.23%; v_{\max} (neat) 3 000, 1 650, 1 264, 1 036, 1 010, 988, and 822 cm⁻¹; $\delta_{\text{H}}(\text{CCl}_4)$ 1.27 (6 H, t, *J* 7 Hz, 2 × CH₂CH₃), 1.32 (3 H, d, *J* 7 Hz, CHCH₃), 3.96 (4 H, quin, *J* 7 Hz, 2 × CH₂CH₃), 4.79 (1 H, m, CHCH₃), 4.90–5.40 (2 H, m, CH=CH₂), and 5.55–6.15 (1 H, m, CH=CH₂); *m/z* 208 (*M*⁺) and 155 (100%).

Transition-metal-catalysed Reaction of the Phosphate (1) with Phenylmagnesium and Hexylmagnesium Bromides.—The following examples represent the general procedure.

(a) To a solution of phenylmagnesium bromide, prepared from magnesium (120 mg, 5 mg-atom) and bromobenzene (0.53 ml, 5 mmol) in diethyl ether (5 ml), was added copper(I) iodide (94 mg, 0.5 mmol) and the mixture was stirred at 0 °C for 10 min. A solution of the phosphate (1) (624 mg, 3 mmol) in diethyl ether (5 ml) was then added at 0 °C and the mixture was left overnight at room temperature. The reaction was quenched by the addition of water and the products were extracted with diethyl ether. The extracts were dried (Na₂SO₄) and the solvent was evaporated. The residue was Kugelrohr distilled (b.p. 115 °C/21 mmHg) to give an oil (344 mg, 87%) which was analysed by g.l.c. (Apiezon grease L; 2 m; 130 °C) and shown to be a mixture of 90% of (2; R = Ph) (*E:Z* 68:32) and 10% of (3; R = Ph). Each component was separated by preparative g.l.c. and characterized by spectroscopic data. Results for other catalysts are summarized in the Table. 1-Phenylbut-2-ene (2; R = Ph),¹² $\delta_{\text{H}}(\text{CCl}_4)$ 1.69 (3 H, m, CH₃), 3.23 (2 H, m, CH₂), 5.49 (2 H, m, CH=CH), and 7.10 (5 H, m, Ph). 3-Phenylbut-1-ene (3; R = Ph),¹² $\delta_{\text{H}}(\text{CCl}_4)$ 1.34 (3 H, d, *J* 7 Hz, CH₃), 3.40 (1 H, quin, *J* 7 Hz, 3-H), 4.75–5.15 (2 H, m, CH=CH₂), 5.68–6.28 (1 H, m, CH=CH₂), and 7.12 (5 H, m, Ph).

(b) Reactions with hexylmagnesium bromide were similarly carried out. Dec-2-ene (2; R = hexyl),¹³ $\delta_{\text{H}}(\text{CCl}_4)$ 0.90 (3 H, m, CH₃), 1.28 (10 H, br s, 5 × CH₂), 1.62 (3 H, br s, CH₃), 1.98 (2 H, m, CH₂), and 5.32 (2 H, m, 2 × CH). 3-Methylnon-1-ene (3; R = hexyl),¹⁴ $\delta_{\text{H}}(\text{CCl}_4)$ 0.90 (3 H, m, CH₂CH₃), 0.95 (3 H, d, *J* 7 Hz, CHCH₃), 1.25 (10 H, br s, 5 × CH₂), 2.10 (1 H, m, 3-H), 4.65–5.05 (2 H, m, CH=CH₂), and 5.35–5.95 (1 H, m, CH=CH₂).

1-Benzoyloxymethyl-2-methylprop-2-enyl Diethyl Phosphate (5).—To a solution of the allylic alcohol (4)⁹ (1.6 g, 8.3 mmol) in pyridine (2 ml) was added dropwise diethyl phosphorochloridate (1.3 ml, 9 mmol) at 0 °C and the mixture was stirred for 3 h. The reaction mixture was then poured into sulphuric acid (1M; 100 ml), and extracted with diethyl ether. The extracts were washed in turn with aqueous sodium hydrogen carbonate and brine, and dried (Na₂SO₄). Evaporation of the solvent gave crude (5) as an oil (2.61 g, 96%). Column chromatography on silica gel with diethyl ether as eluant gave pure (5) (1.96 g, 71%) (Found: C, 58.75; H, 7.9. C₁₆H₂₅O₅P requires C, 58.53; H, 7.67%; v_{\max} (neat) 3 000, 1 656, 1 452, 1 370, 1 262, 1 200, 742, and 700 cm⁻¹; $\delta_{\text{H}}(\text{CCl}_4)$ 1.20 (6 H, dt, *J* 7 and 2 Hz, 2 × CH₂CH₃), 1.70 (3 H, s, CH₃), 3.50 (2 H, d, *J* 6 Hz, CHCH₂),

3.94 (4 H, quin, *J* 7 Hz, 2 × CH₂CH₃), 4.47 (2 H, s, CH₂Ph), 4.72 (1 H, m, CHCH₂), 4.80–5.10 (2 H, m, =CH₂), and 7.19 (5 H, m, Ph); *m/z* 328 (*M*⁺) and 155 (100%).

Copper(I)-catalysed Reaction of the Phosphate (5) and 3-Methylbut-2-enylmagnesium Chloride.—A solution of 1-chloro-3-methylbut-2-ene (526 mg, 5 mmol) in diethyl ether (10 ml) was added dropwise to a suspension of magnesium turnings (240 mg, 10 mg-atom) in diethyl ether (10 ml) cooled in an ice-salt bath. After the addition was complete, the mixture was further stirred for 1 h. The solution of 3-methylbut-2-enylmagnesium chloride thus prepared was added to a suspension of copper(I) iodide (96 mg, 0.5 mmol) in diethyl ether (2 ml) at 0 °C, and the mixture was stirred for 15 min. To this mixture was added a solution of the phosphate (5) (656 mg, 2 mmol) in diethyl ether (5 ml) at 0 °C, and the entire mixture was warmed to room temperature and left overnight. After the addition of saturated aqueous ammonium chloride, the products were extracted with diethyl ether, washed with brine, and dried (Na₂SO₄). The solvent was evaporated and the residue was Kugelrohr distilled (b.p. 140 °C/5 mmHg) to give a mixture of the dienes (6) and (7) (430 mg, 88%). Gas chromatographic analysis (Apiezon grease L; 1 m; 200 °C) revealed that the ratio (6):(7) was 84 (*E:Z* 78:22):16. When the reaction was conducted in THF, a mixture of (6) and (7) [97 (*E:Z* 83:17):3] was obtained in 51% yield. Pure samples of (6) and (7) were obtained by preparative g.l.c. The spectroscopic data (i.r. and ¹H n.m.r.) of (6) were in accord with those of an authentic sample prepared from geraniol. Benzyl geranyl ether (6) had $\delta_{\text{H}}(\text{CCl}_4)$ 1.60 (6 H, s, 2 × CH₃), 1.66 (3 H, s, CH₃), 2.02 (4 H, m, [CH₂]₂), 3.92 (2 H, d, *J* 7 Hz, CHCH₂O), 4.40 (2 H, s, CH₂Ph), 6.05 (1 H, br s, CH=), 5.33 (1 H, br t, *J* 7 Hz, CH=), and 7.20 (5 H, s, Ph). Benzyl 2-isopropenyl-5-methylhex-4-enyl ether (7) (Found: C, 83.25; H, 9.85. C₁₇H₂₄O requires C, 83.55; H, 9.90%; v_{\max} (neat) 2 930, 1 642, 1 450, 1 376, 1 360, 1 108, 889, 734, and 698 cm⁻¹; $\delta_{\text{H}}(\text{CCl}_4)$ 1.58 (3 H, s, CH₃), 1.67 (6 H, s, 2 × CH₃), 2.15 (3 H, m, CH, and 3-H₂), 3.35 (2 H, d, *J* 7 Hz, CHCH₂O), 4.42 (2 H, s, CH₂Ph), 4.70 (2 H, m, =CH₂), 5.00 (1 H, br t, *J* 7 Hz, 4-H), and 7.20 (5 H, m, Ph); *m/z* 244 (*M*⁺) and 91 (100%).

Debenzylation of (6); Synthesis of Geraniol (8).—A solution of the 97:3 mixture of (6) and (7) (180 mg, 0.74 mmol), obtained from the above reaction in THF, in THF (2 ml) was added to a suspension of lithium (65 mg, 9.3 mg-atom) in ethylamine (10 ml) at -78 °C and the reaction mixture was vigorously stirred at that temperature for 20 min. The blue reaction mixture was quenched by the addition of isoprene (0.5 ml) followed by ethanol (2 ml) at -78 °C. The mixture was poured into water, extracted with diethyl ether, washed with brine, and dried (Na₂SO₄). The solvent was evaporated and the residue was chromatographed on silica gel with diethyl ether as eluant to afford geraniol (8) (92 mg, 81%). G.l.c. analysis (PEG; 150 °C) revealed that the *E:Z* ratio was 83:17. The spectroscopic data (i.r. and ¹H n.m.r.) of the geraniol obtained were in accord with those of an authentic sample.

The debenzylation product of (7) could not be isolated.

Copper(I)-catalysed Reaction of the Phosphate (5) and 3-Methylbut-3-enylmagnesium Bromide.—A solution of 4-bromo-2-methylbut-1-ene (1.49 g, 10 mmol) in diethyl ether (6 ml) was added dropwise to a suspension of magnesium turnings (240 mg, 10 mg-atom) in diethyl ether (4 ml) cooled in an ice-bath. After the addition was complete, the mixture was stirred at 0 °C for 2 h and then at room temperature for 30 min. The solution of 3-methylbut-3-enylmagnesium bromide thus prepared was diluted by the addition of diethyl ether (10 ml) and then added to a suspension of copper(I) iodide (190 mg, 1 mmol) in diethyl ether (2 ml) at 0 °C, and the mixture was stirred for 20 min. To

this mixture was added a solution of the phosphate (5) (1.31 g, 4 mmol) in diethyl ether (6 ml) at 0 °C, and the entire mixture was stirred at room temperature for 3 h. The reaction mixture was poured into aqueous ammonium chloride and the products were extracted with diethyl ether. The extracts were washed with brine, dried over Na₂SO₄, and evaporated. The residue was Kugelrohr distilled (b.p. 140 °C/4 mmHg) to give a mixture of the dienes (9) and (10) (886 mg, 91%). Gas chromatographic analysis (Apiezon grease L; 1 m; 200 °C) revealed that the ratio (9):(10) was 95 (*E*:*Z* 61:39):5. When the reaction was carried out in THF, a mixture of (9) and (10) [(9):(10) 94 (*E*:*Z* 77:23):6] was obtained in 91% yield. Pure sample of (9) and (10) were isolated by preparative g.l.c. Benzyl 3,7-dimethyloct-2,7-dienyl ether (9) (Found: C, 83.3; H, 10.0. C₁₇H₂₄O requires C, 83.55; H, 9.90%; ν_{\max} (neat) 2 950, 1 650, 1 454, 1 376, 1 072, 890, 738, and 700 cm⁻¹; δ_{H} (CCl₄) 1.65 (6 H, m, 2 × CH₃), 1.30—2.20 (6 H, m, [CH₂]₃), 3.94 (2 H, d, *J* 7 Hz, CHCH₂O), 4.42 (2 H, s, CH₂Ph), 4.65 (2 H, br s, =CH₂), 5.35 (1 H, br t, *J* 7 Hz, =CH), and 7.24 (5 H, m, Ph); *m/z* 244 (*M*⁺) and 91 (100%). Benzyl 2-isopropenyl-5-methylhex-5-enyl ether (10) (Found: C, 83.3; H, 10.2. C₁₇H₂₄O requires C, 83.55; H, 9.90%; ν_{\max} (neat) 2 930, 1 644, 1 450, 1 372, 1 360, 1 114, 888, 734, and 698 cm⁻¹; δ_{H} (CCl₄) 1.68 (6 H, br s, 2 × CH₃), 1.30—2.50 (5 H, m, 2-H and [CH₂]₂), 3.35 (2 H, d, *J* 7 Hz, CHCH₂O), 4.43 (2 H, s, CH₂Ph), 4.70 (4 H, m, 2 × =CH₂), and 7.18 (5 H, m, Ph); *m/z* 244 (*M*⁺) and 91 (100%).

Benzyl 8-Hydroxy-3,7-dimethyloct-2-enyl Ether.—A solution of the 94:6 mixture of (9) and (10) (728 mg, 2.98 mmol) in THF was added to a solution of 9-borabicyclo[3.3.1]nonane (336 mg, 3 mmol) in THF (3 ml) at 0 °C, and the reaction mixture was left overnight at room temperature. A solution of sodium hydroxide (120 mg, 3 mmol) in water (1 ml) and then hydrogen peroxide (30%; 1.06 ml, 10.8 mmol) were cautiously added to the reaction mixture at 0 °C. After being stirred at room temperature for 1 h, the mixture was poured into water and extracted with diethyl ether. The extracts were dried (Na₂SO₄) and evaporated. The residue was chromatographed on silica gel [benzene–diethyl ether (1:1)] to afford the hydroxy ether (11) (675 mg, 86%) (Found: C, 77.15; H, 10.3. C₁₇H₂₆O₂ requires C, 77.82; H, 9.99%; ν_{\max} 3 400, 2 930, 1 665, 1 452, 1 376, 1 360, 1 060, 743, and 696 cm⁻¹; δ_{H} (CCl₄) 0.87 (3 H, d, *J* 7 Hz, CHCH₃), 1.10—1.80 (5 H, m, CH and 2 × CH₂), 1.60 (3 H, s, CH₃), 1.99 (2 H, m, CH₂), 2.40 (1 H, br s, OH), 3.30 (2 H, d, *J* 7 Hz, CH₂OH), 3.93 (2 H, d, *J* 7 Hz, CH₂OCH₂Ph), 4.43 (2 H, s, CH₂Ph), 5.33 (1 H, br t, *J* 7 Hz, =CH), and 7.22 (5 H, m, Ph); *m/z* 262 (*M*⁺) and 108 (100%). The *E*:*Z* ratio was 79:21 by g.l.c. (SE-30; 200 °C).

3,7-Dimethyloct-2-ene-1,8-diol (12).—A solution of the ether (11) (183 mg, 0.7 mmol) in THF (2 ml) was added to a mixture of lithium (70 mg, 10 mg-atom) and ethylamine (10 ml) at –78 °C. When the mixture was warmed to –30 °C, the reaction started and a blue colour developed. The mixture was recooled to

–78 °C and stirred at that temperature for 10 min. The reaction was quenched by the addition of isoprene (0.5 ml) and ethanol (2.0 ml). The mixture was poured into water and extracted with diethyl ether. The extracts were washed with brine and dried (Na₂SO₄). Evaporation and column chromatography on silica gel (diethyl ether as eluant) afforded the diol (12) (90 mg, 75%) as an oil. The *E*:*Z* ratio was 76:24 by g.l.c. (PEG; 175 °C). The spectroscopic data (¹H n.m.r.) of (12) were consistent with those of the natural product reported in the literature:¹¹ ν_{\max} (neat) 3 330, 2 930, 1 665, 1 458, 1 380, 1 040, 1 025, 1 000, and 730 cm⁻¹; δ_{H} (CDCl₃) 1.90 (3 H, d, *J* 7 Hz, CHCH₃), 1.10—1.80 (5 H, m, CH and 2 × CH₂), 1.66 (3 H, s, CH₃), 2.00 (2 H, m, CH₂), 3.00 (2 H, s, 2 × OH), 3.43 [2 H, d, *J* 7 Hz, CH(CH₃)CH₂OH], 4.13 (2 H, d, *J* 7 Hz, =CHCH₂OH), and 5.40 (1 H, t, *J* 7 Hz, =CH); *m/z* 154 (*M*⁺ – H₂O) and 71 (100%).

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