

Terpenoids: Part. LXX. A Synthesis of Myrcenol

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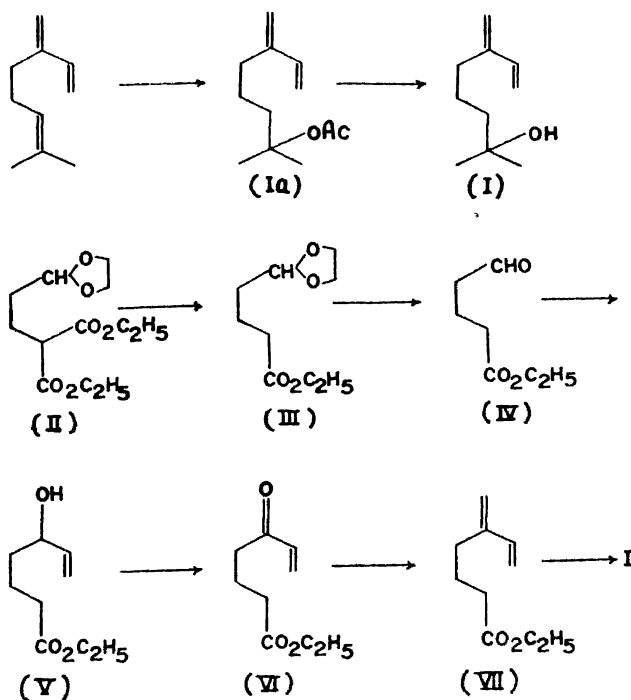
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Ethyl 5-keto-6-heptenoate, obtained by the action of vinyl magnesium bromide on ethyl 4-formyl butanoate and oxidation of the resulting alcohol with Jones' reagent, was submitted to the Wittig reaction with methylenetriphenylphosphorane to afford ethyl 5-methylene-6-heptenoate. Gignard reaction with methyl magnesium iodide on the diene-ester furnished myrcenol.

Myrcenol, an acyclic monoterpene alcohol, was obtained by sulphuric acid-catalysed addition of acetic acid¹ to β -myrcene followed by the hydrolysis of the intermediate acetate (Ia).

Structure (I), proposed for this hydration product of β -myrcene, was established through its spectral data and chemical properties¹. The present communication reports a direct synthesis of myrcenol through the sequence of reaction depicted in the chart given below :



One of the carbethoxy groups of the substituted malonic ester² (II) was eliminated by heating it with sodium cyanide in dimethyl sulphoxide³ to give the monoester (III) in 50% yield. This was deketalised with *p*-toluene-sulphonic acid in aqueous acetone to furnish, after purification, the aldehyde (IV) in 64% yield. Action of vinyl magnesium bromide on the aldehyde (IV), in tetrahydrofuran, generated ethyl 5-hydroxy-6-heptenoate (V) in 47% yield. Oxidation of the allylic alcohol (V) with Jones' reagent⁴, gave after usual purification, the unsaturated ketone (VI) in 46% yield.

The vinyl ketone (VI) when subjected to Wittig reaction⁵ with methylenetriphenylphosphorane afforded the conjugated diene (VII) in 68.5% yield after purification by chromatography over alumina. The product was found to be homogeneous (t.l.c.). The compound (VII) was finally transformed into the title compound by treatment with methylmagnesium iodide in dry ether. The product was purified by fractional distillation under reduced pressure and the purity checked by t.l.c. The identity of the synthetic alcohol (I) was established by comparison of its I.R. and U.V. data with that reported in the literature¹.

EXPERIMENTAL

b.ps. are uncorrected. Microanalysis by L. K. Khullar, Microanalyst, Panjab University, Chemistry Department, Chandigarh. I.R. Spectra recorded on Perkin-Elmer Infra-red spectrophotometer with sodium chloride optics using thin liquid films.

Ethyl 5,5-ethylenedioxy pentanoate (III) : A mixture of the diester (II, 55 g.) dimethylsulphoxide (150 ml) and sodium cyanide (20 g) was heated at 160–70° for 4 hr. Thereafter, the mixture was cooled, poured into cold water and extracted with petroleum ether (60–80°). The combined extract was washed thoroughly with water and dried. After the removal of the solvent, the residue was distilled under reduced pressure to give the monoester (III), b.p. 112–15°/5 mm; yield 20 g (50%); η_D^{30} 1.4435; (Found C, 57.51; H, 8.34. $C_9H_{16}O_4$ requires C, 57.43; H, 8.57%). I.R. Spectrum had prominent peaks at 1730, 1450, 1340, 1170, 1145, and 1040 cm^{-1} .

Ethyl 4-formyl butanoate (IV) : The ketal (III, 10 g) was mixed with *p*-toluene-sulphonic acid (6.0 g), acetone (480 ml.) and water (60 ml.) and the reaction mixture was stirred at room temperature for 3 hr. The excess of PTS was destroyed by washing with sodium chloride saturated solution of sodium bicarbonate (5%). Acetone was removed under low pressure and the residue was extracted with ether. The ethereal extract was washed with water and dried over sodium sulphate. The solvent was evaporated and the residual oil distilled under reduced pressure to afford aldehyde-ester (IV), b.p. 85°/5 mm; yield 4.9 g (64.5%), η_D^{30} 1.4440. I.R. spectrum showed characteristic peaks at 2730, 1730, 1440, 1350, 1300, 1170, 1080, 1070, 1020, 935 and 855 cm^{-1} . (Found : C, 58.45; H, 8.30. $C_7H_{12}O_3$ requires C, 58.33; H, 8.33%).

Ethyl 5-hydroxy-6-heptenoate (V) : Grignard reagent was prepared from magnesium (2.8 g) and vinyl bromide (13 g.) in dry tetrahydrofuran (75 ml) and was added dropwise to a solution of aldehyde (IV, 14.4 g) in tetrahydrofuran (100 ml.) in the cold, with stirring. After

the addition was over, the contents were stirred for 4 hr. more and thereafter decomposed with ice-cold solution of ammonium chloride. The organic phase was separated and the aqueous layer extracted with ether (4×50 ml). The total THF-ether extract was dried and solvent expelled. The residual oil was distilled under reduced pressure to obtain the allylic alcohol (V); b.p. 100°/5 mm; yield 8 g (47%); η_D^{30} 1.4515. I.R. spectrum showed prominent bands at 3450, 3050, 1730, 1640, 1440, 1350, 1240, 1170, 1055, 1020, 915, 845, and 740 cm^{-1} . (Found: C, 62.57; H, 9.18. $\text{C}_9\text{H}_{16}\text{O}_3$ requires C, 62.76; H, 9.36%).

Ethyl 5-oxo-6-heptenoate (VI): The Jones' reagent (12.10 ml.) was added in small portions at a time to an ice-cold solution of carbinol (V, 7.75 g.) in acetone (60 ml.). The reaction mixture was stirred for half an hour, diluted with saturated solution of sodium chloride and extracted thoroughly with ether. The ethereal phase was washed with sodium bicarbonate solution (5%) and dried (Na_2SO_4). The solvent was removed and the residue chromatographed over neutral alumina (with benzene-petroleum ether, 1 : 4), and thereafter distilled under reduced pressure to give the unsaturated ketone (VI), b.p. 90–95°/5 mm; yield 3.7 g. (46.7%), η_D^{30} 1.4615. Thin layer chromatography gave single spot (chloroform petroleum ether 1 : 1), R_f 0.65. (Found: C, 63.70; H, 8.35. $\text{C}_9\text{H}_{14}\text{O}_3$ requires C, 63.51; H, 8.29%). I.R. Spectrum showed prominent peaks at 3050, 1725, 1685, 1645, 1445, 1350, 1180, 1080, 1020, 990, 910, 850 and 750 cm^{-1} .

Ethyl 5-methylene-6-heptenoate (VII): Methylenetriphenylphosphorane was prepared from sodium hydride (1.25 g.) in dimethylsulphoxide (12.5 ml.) and methyltriphenylphosphonium iodide (10.5 g.) in dimethylsulphoxide (25 ml.) under nitrogen atmosphere. To this was added the unsaturated ketone (VI, 3.4 g.) in tetrahydrofuran (15 ml.), below 15°. The contents were stirred at room temperature for 2 hr. and then left overnight. The reaction mixture was poured into iced water and extracted with petroleum ether. The extract were washed with water and dried. After the removal of solvent the residue was passed through neutral alumina, eluting with 10% benzene-petroleum ether. Subsequent distillation under reduced pressure afforded the diene (VII), b.p. 90–95°/5 mm., yield 2.1 g (62.1%); t.l.c. gave a single spot, R_f 0.82 (solvent system; *n*-hexane-chloroform, 1 : 1). I.R. spectrum showed characteristic peaks at 3055, 1735, 1635, 1600, 1460, 1350, 1250, 1180, 1030, 990, 890 and 750 cm^{-1} . (Found: C, 71.76; H, 9.37. $\text{C}_{10}\text{H}_{16}\text{O}_2$ requires C, 71.39; H, 9.59%).

3-Methylene-7-methyl-1-octen-7-ol (I): To the Grignard reagent, prepared from magnesium (0.9 g) and methyl iodide (6 g.) in dry ether (50 ml.) was added dropwise the ester (VII, 2 g.) in dry ether (20 ml.) and stirred the reaction mixture for 1 hr. After heating under mild reflux for 2 hr. it was allowed to stand overnight at room temperature. The reaction mixture was decomposed with cold solution of ammonium chloride and worked up in usual manner. The residue left after the removal of solvent was distilled under reduced pressure to furnish the title compound (I) b.p. 90–92°/10 mm; yield 1.2 g. (66.5%), η_D^{30} 1.4472. Lit.¹ reports η_D^{20} 1.4490. I.R. spectrum showed peaks at 3350, 3050, 1800, 1640, 1605, 1460, 1365, 1200, 1140, 995, 905, 890 and 750 cm^{-1} which are comparable with those reported in the literature¹. $\lambda_{max}^{ethanol}$ 225 $\text{m}\mu$ ($\epsilon = 14,800$), Lit.¹ reports $\lambda_{max}^{ethanol}$ 225 $\text{m}\mu$ ($\epsilon = 15,500$). (Found: C, 78.15; H, 11.57. $\text{C}_{10}\text{H}_{18}\text{O}$ requires C, 77.86; H, 11.76%).

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