Synthesis of (+)-Hinesol and 10-epi-(+)-Hinesol

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Summary The synthesis of (+)-hinesol (**1**) and 10-epi-hinesol from (−)-β-pinene is described.

Since the revision of the structures of the vetivane sesquiterpenes[1a] from hydroazulenes to spiro[4,5]decane skeletal types[1b] there have been a number of syntheses reported.[2a] Recently the first synthesis of optically active spiro[4,5]-decanes was described.[2b] As an extension of our previous work utilising (−)-β-pinene to synthesise the boll weevil pheromone we now report the synthesis of (+)-hinesol (**1**) and 10-epi-hinesol from (−)-β-pinene. Conversion of (−)-β-pinene into the ether (**2**) was accomplished by standard methods.[3] Conversion of (**2**) into (**3**) *via* the tosylate (*i.e.* $LiAlH_4$, TsCl–py, NaCN–Me_2SO, NaOH, MeOH–amberlite resin IR-120H) gave (**3**) in an overall yield of 66%. Treatment of (**3**) with $BF_3.OEt_2$–Ac_2O at 0 °C gave the 8-substituted fenchane (**4**; R = Ac) (⩾ 95%) in accordance with previous work.[4] Acid hydrolysis (MeOH–H^+) of (**4**; R = Ac) gave (**4**; R = H) (98%) which was converted (Me_2CO–$CuSO_4$) into the acetonide (**4**; R,R = $>CMe_2$). Dehydration of (**4**; R,R = $>CMe_2$) using the recently developed selenium reagents[5] [$LiNPr_2^i$, $(PhSe)_2$, $NaIO_4$] gave, exclusively, the *E*-enone (**5**) (⩾ 90%). Dimethylcopperlithium[6] reacted with the enone (**5**) to give a 1 : 1 mixture of the methyl epimers (**6**) (95%), τ 9·1 and 9·05 (2 doublets *J* 6Hz). Conversion of the ester (**6**) into the sulphone (**7**) was achieved in 69% yield ($LiAlH_4$, TsCl–py, $MeSO_2Ph$–NaH). Removal of the acetonide protecting group in (**7**), tosylation of the primary hydroxyl (TsCl–py), followed by Collins oxidation[7] gave the ketotosylate (**8**) (⩾ 80%). Fragmentation of (**8**) in the previously established manner[8] (model studies) using NaH–Me_2SO at room

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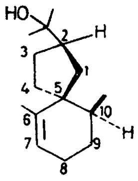

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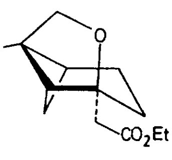

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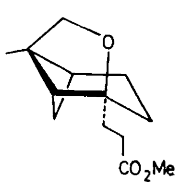

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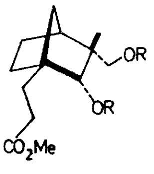

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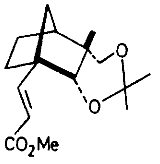

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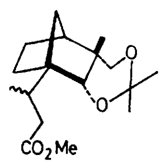

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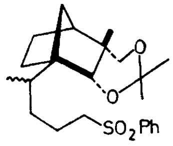

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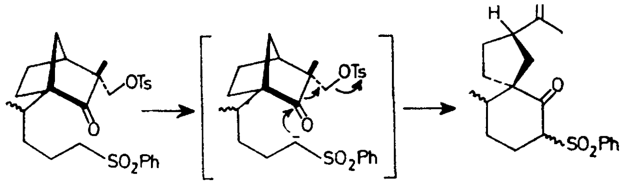
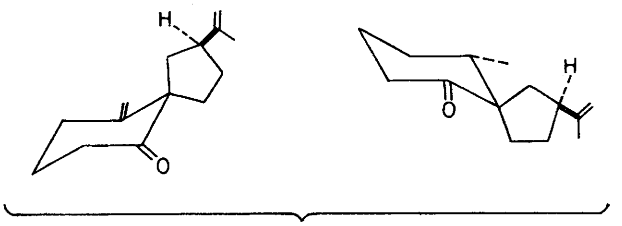


(8) (9)

temperature gave the spiro[4,5]decane (**9**) (65%), and a by-product.‡ Reductive cleavage of the phenylsulphonyl function using aluminium amalgam[9] in wet THF gave the ketone (**10**). N.m.r. shift reagent studies indicated that (**10**) consisted of a mixture of epimers with the methyl group equatorial in both isomers. The ketone (**10**) was treated with MeMgI to provide the tertiary carbinol which was epoxidised using *m*-chloroperbenzoic acid in THF containing aqueous sodium hydrogen carbonate (to prevent any acid-catalysed cyclisations) to give the epoxide (**11**) (88%). The epoxide (**11**) crystallised at room temperature. Dehydration of crystalline (**11**) using the Burgess[10] reagent ($MeO_2CN^-SO_2N^+Et_3$) gave the olefin (**12**), along with the *exo*-isomer (2:1). Treatment of (**12**) with $LiAlH_4$ gave (+)-hinesol (**1**)§ and 10-epi-hinesol as a 1:1 mixture ($[\alpha]_D^{25}$ + 35·4°) (lit.[1,2] for (−)-hinesol $[\alpha]_D^{25}$ −40° and −48°). Since the acetates of (**1**) and its 10-epimer are known, and separable (v.p.c.) this constitutes a synthesis of the optically active spiro[4,5]decanes (+)-hinesol and 10-epi-hinesol from (−)-β-pinene.[11] The separation of 10-methyl epimers at an earlier stage and proof of configuration will be the subject of a full paper.



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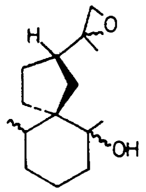

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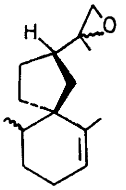

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All new compounds gave satisfactory spectral¶ and microanalytical data.

(*Received*, 23*rd September* 1975; *Com.* 1091.)

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‡ The structure of this material will be discussed in a subsequent paper.

§ (+)-Hinesol is the mirror image of the natural isomer.[8]

¶ We thank Professor J. A. Marshall for supplying spectra of authentic (±)-hinesol.

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[11] Presented, in part, at The Third International Symposium on Synthesis in Organic Chemistry, Oxford 1973.