SYNTHESIS OF E/Z-SESQUILAVANDULOLS FROM THE PRODUCT OF THE ENE REACTION OF LAVANDULYL ACETATE WITH PHENYLSULFINYL CHLORIDE

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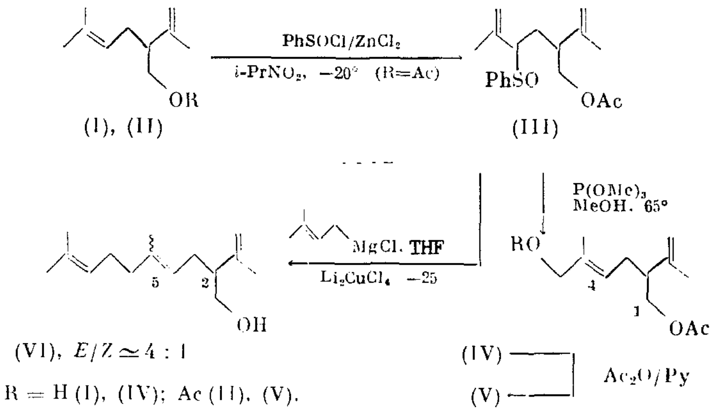
The ene reaction of (±)-lavandulyl acetate with PhSOCl catalyzed by $ZnCl_2$ proceeds highly selectively at the isopropylidene fragment of this molecule to give the corresponding allyl sulfoxide. The sulfoxide–sulfenate rearrangement of this product and its one-step conversion to a mixture of racemic E/Z-sesquilavandulols were studied.

We have recently shown that the reaction of regular linear isoprenoids with PhSOCl catalyzed by $ZnCl_2$ proceeds as a chemically specific and regiospecific ene reaction involving the trisubstituted double bond of the isopropylidene fragment of such oligoolefins [1,2]. In the present communication, we consider the application of this reaction for the selective functionalization of an irregular plant monoterpenol, namely, lavandulol (I) [3], which provides simple access to its natural isoprenolog, sesquilavandulol.

In accord with available data [1,2], the low-temperature treatment of acetate (II) of readily available (±)-lavandulol (I) by a mixture of about 1.5 molar equivalents of PhSOCl and $ZnCl_2$ in i-$PrNO_2$ gives allyl sulfoxide (III) in high yield. Sulfoxide (III) arises as a result of the selective electrophilic attack of the trisubstituted double bond in starting (II) rather than the disubstituted double bond.

The structure of moderately stable sulfoxide (III) isolated by flash chromatography on silica gel as a mixture of diastereomers was supported by its physicochemical indices and the comparison of these indices with the available data for related isoprenoid allyl sulfoxides [1,2]. For example, the PMR spectrum of (III) has partially overlapped, broadened signals of the four exo-methylene protons at δ 4.6-5.1 as well as a multiplet for HCS at δ 3.0-3.3 ppm.

The sulfoxide–sulfenate rearrangement of (III) under our previous conditions [1,2] leads almost quantitatively to allylic acetoxyalcohol (IV), additionally characterized as diacetate (V). The E configuration of the trisubstituted C=C bond of both these compounds



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was assigned on the basis of the available data on the stereochemistry of this rearrangement [1,2,4], which was indicated by the observation of a broadened singlet in the PMR singlet for the CH_3-C^5 group at δ 1.58 ppm. This signal is shifted downfield in the case of (V) by Δδ 0.1 ppm. The position of the signal for the methyl group of the isopropenyl fragment, δ 1.64 ppm, is virtually invariant in the spectra of (IV) and (V).

Derivatives (III)-(V) of lavandulol (I), which now prove readily available, may be used as intermediates in the total synthesis of higher prenologs of (I), some of which have recently been isolated from plant sources [5,6] and synthesized [7,8].

As an illustration, we examine the preparation of racemates of E- and Z-sesquilavandulol (VI) found in the roots of *Peucedanum palustre* [6]. Thus, the Wurtz cross coupling of sulfoxide (III) with excess prenylmagnesium chloride catalyzed by the Kochi reagent and occuring by the scheme S_N2' [2,9] gives (±)-(VI) in good yield as a mixture of stereoisomers 4E/4Z ≈ 4:1 as indicated by gas–liquid chromatography and PMR spectroscopy. The structures of these stereoisomers were supported spectrally taking account of the data reported for these compounds.

In conclusion, we note that the absolute configuration of these sesquiterpenoids, which has still not been elucidated, may be readily established starting from chiral lavandulol (I) and the data presented in this work.

EXPERIMENTAL

The IR spectra for $CHCl_3$ solutions were obtained on a UR-20 spectrometer. The PMR spectra for $CDCl_3$ solutions were taken on a Bruker WM-250 spectrometer. The mass spectra were taken on a Varian MAT CH-6 mass spectrometer at 70 eV. The R_f values are given for Silufol silica gel plates using 1:4 hexane–ether as the eluent.

2-Isopropenyl-5-methyl-4-phenylsulfenyl-5-hexen-1-ol Acetate (III). A sample of 1.51 g (11.1 mmoles) $ZnCl_2$ and one portion of 1.78 g (11.1 mmoles) PhSOCl [10] were added consecutively to a solution of 1.45 g (7.4 mmoles) (II) [3] in 15 ml i-$PrNO_2$ stirred at −50°C in an argon atmosphere. The reaction mass was warmed over 20 min to −20°C, stirred at this temperature for 2 h, and then decomposed at −50°C by the addition of a solution of 1.3 g (16.4 mmoles) pyridine in 10 ml ether. The precipitate was filtered off and washed on the filter with ether. The combined filtrate was washed with water, dried over $MgSO_4$, and evaporated in vacuum. The residue (~3 g) was subjected to chromatography on 80 g silica gel. Gradient elution from hexane to ether gave 1.66 g (70%) (III) as a colorless oil, R_f 0.37. IR spectrum (ν, cm^{-1}): 900, 1050, 1090, 1230, 1360, 1380, 1440, 1650, 1740, 2970, 3040, 3080. PMR spectrum (δ, ppm): 1.45, 1.50, 1.59, and 1.69 br.s (6H, CH_3), 1.6-2.4 m (3H, HC^2, HC^3), 2.0 s (3H, CH_3CO), 3.0-3.3 m (1H, HCS), 4.0 m (2H, CH_2O), 4.6-5.1 m (4H, H_2C=C), 7.4-7.7 m (5H, C_6H_5). Mass spectrum (m/z): 320 (M^+), 195, 149, 135, 107, 93, 79, 68. Molecular weight calculated for $C_{18}H_{24}O_3S$: 320.5.

2-Isopropenyl-5-methyl-6-hydroxy-4E-hexen-1-ol Acetate (IV). A solution of 0.2 g (0.62 mmole) (III) and 0.25 g (1.93 mmoles) $P(OMe)_3$ in 3 ml methanol was heated in an argon atmosphere at 65°C for 2 h and then evaporated in vacuum. The residue (~0.2 g) was subjected to chromatography on 10 g silica gel. Gradient elution from hexane to 3:2 hexane–ether gave 0.12 g (91%) (IV) as a colorless oil, R_f 0.48. IR spectrum (ν, cm^{-1}): 895, 1040, 1240, 1365, 1370, 1375, 1450, 1650, 1740, 2920, 2950, 3080, 3470, 3620. PMR spectrum (δ, ppm, J, Hz): 1.58 and 1.64 br.s (6H, CH_3), 1.97 s (3H, CH_3CO), 2.0-2.4 m (3H, HC^2, HC^3), 3.91 br.s (2H, HC^6), 3.99 d (2H, HC^1, J = 6.5), 4.69 and 4.78 br.s (2H, H_2C=C), 5.29 br.t (1H, HC^4, J = 7). Mass spectrum (m/z): 152 $(M - AcOH)^+$, 134, 121, 119, 93, 67. Calculated for $C_{12}H_{20}O_3$: mol. mass 212.3.

Diacetate (V) was obtained as a colorless liquid, bp 91-93°C (0.08 mm), n_D^{20} 1.4666. IR spectrum (ν, cm^{-1}): 900, 1025, 1230, 1370, 1380, 1450, 1650, 1745, 2940, 3080. PMR spectrum (δ, ppm, J, Hz): 1.64 and 1.68 br.s (6H, CH_3), 2.03 and 2.06 s (6H, CH_3CO), 2.1-2.4 m (3H, HC^2, HC^3), 4.03 d (2H, HC^1, J = 6.5), 4.43 br.s (2H, HC^6), 4.74 and 4.84 br.s (2H, H_2C=C), 5.39 br.t (1H, HC^4, J = 7). Found: C, 66.41; H, 8.82%; 254 (M^+). Calculated for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72%; mol. mass 254.3.

(±)-Sesquilavandulol (VI). A sample of 0.5 ml 0.1 M Li_2CuCl_4 in THF (0.05 mmole) was added to a solution of 0.72 g (2.25 mmoles) (III) in 6 ml THF at −25°C in an argon atmosphere and the mixture was stirred for 30 min. Then, 11.3 ml of 1.2 M (13.6 mmoles) prenylmagnesium chloride in THF was added. The reaction solution was stirred at −25°C for 10 min and then warmed to 0°C over 30 min. The reaction mixture was decomposed by the addition of aqueous ammonium chloride. The aqueous layer was separated and extracted with ether. Ordinary treatment of the combined extract gave about 1 g crude product, which was subjected to chromatography on 30 g silica gel. Gradient elution from hexane to 7:3 hexane–ether gave 0.22 g

(44%) (VI) as a colorless liquid, bp 81-82°C (0.08 mm), n_D^{20} 1.4854 [7,8]. The sample of (VI) contained up to 20% of the 4Z isomer as indicated by gas–liquid chromatography and PMR spectroscopy.

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CONVERGENT SYNTHESIS OF THE TETRACYCLIC BCDE STRUCTURAL FRAGMENT OF RETIGERANIC ACID

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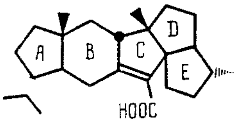
A two-step synthesis was proposed for the tetracyclic triquinane bis-enone from two monocyclic precursors. The bis-enone obtained is a structural fragment of retigeranic acid.

Retigeranic acid (I) is a triquinane sesterterpene isolated from natural sources [1,2].



(I)

The three syntheses which have been reported for this compound may be described by the following schemes:

$$B \longrightarrow AB \longrightarrow AB(C) \longrightarrow AB(C)D(E) \longrightarrow ABCDE\ [3] \qquad (1)$$

where (C) is a six-membered ring subsequently converted to C and (E) is a four-membered ring subsequently converted to E.

$$E \longrightarrow DE \xrightarrow[\overset{\uparrow}{A}]{} CDE \longrightarrow ACDE \longrightarrow ABCDE\ [4] \qquad (2)$$

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