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SYNTHESIS OF (–)-SECOLONGIFOLENE DIOL[1]

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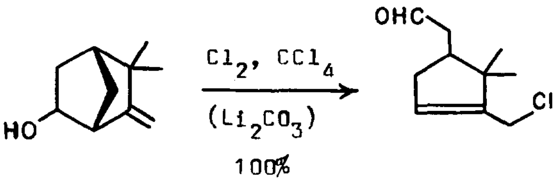
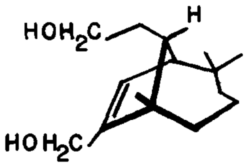
In a recent publication[2], we described a novel fragmentation reaction of certain homoallylic alcohols, as examplified in I → II. We now wish to report the application of this reaction for the synthesis of (–)-secolongifolene diol



I

II



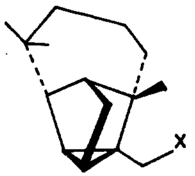
III

(III), optical antipode of a metabolite of the fungus Helminthosporium sativum[3].

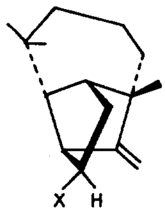
Clearly, the homoallylic alcohol vital to the synthesis of III is 4-hydroxy-longifolene (VII). This intermediate has now been prepared by two routes.

In the first approach, longicyclene (IV)[4] was subjected to NBS cleavage reaction[5], which furnished (100%) a product, consisting essentially of two homoallylic bromides (4:1; PMR), readily recognised on the basis of PMR (splitting pattern of the CHBr signal) as VI (PMR[6]: CHBr, 3.83 ppm, d x d, J_1 = 4Hz, J_2 = 7Hz; ϕ = 85°, 15°, 135°; major product) and IX (PMR: CHBr, 3.70 ppm, d, J ≃ 5Hz; ϕ = 90°, 140°). Hydrolysis of the bromide mixture in aq. dioxane (100°, 24 h) under buffered conditions (Li_2CO_3) gave a product, the PMR spectrum of which indicated it to be a mixture of four alcohols, in which the known[7] ψ-longifolol (V) was present to the extent of 75% and the required alcohol (VII) amounted to some 15% (vide infra).

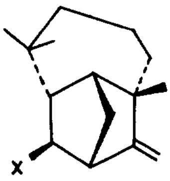
The second route is based on the reasoning that ψ-longifolol (V), under aq. acid-catalysis, should equilibrate, via the cyclopropyl carbinyl cation — homoallylic cation system[8], to furnish a product, in which hopefully some VII (besides X) should be present. In practice, when optically pure (+)-ψ-longifolol (V)[9] was exposed to 0.35% $HClO_4$ in 90% aq. dioxane (45 ± 1°, 12 h)[10], the product consisted of V, VII and X in the approx. ratio (PMR; actual isolation) of 5:2:3. Systematic column chromatography of this product over 15% $AgNO_3$-on-SiO_2 gel led to isolation of the required VII (m.p. 97.5-98.5°; $[\alpha]_D$ + 36.9°, $\underline{c}$ = 2.71%, $CHCl_3$), besides X (m.p. 169-170°; $[\alpha]_D$-24.3°, $\underline{c}$ = 2.47% in $CHCl_3$) and the known ψ-longifolol. Structures VII and X are fully supported by their spectral data: VII (IR[6]: OH 3150, 1055 cm^{-1}; C=C 1650, 892 cm^{-1}. PMR: tert. Me's 0.93, 0.93, 1.01 ppm; C$\underline{H}$OH, 3.82 ppm, d x d, J_1 = 4Hz, J_2 = 7 Hz; C=C$\underline{H}_2$, 1H singlets at 4.70, 4.95 ppm), X (IR: OH 3130, 1038 cm^{-1}; C=C 1650, 885 cm^{-1}. PMR: tert. Me's 1.02, 1.04, 1.04 ppm; C$\underline{H}$OH 3.80 ppm, d, J = 5 Hz, C=C$\underline{H}_2$, 1H singlets at 4.55 and 4.91 ppm).



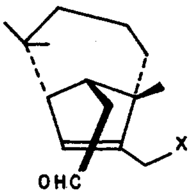
IV: X = H
V: X = OH



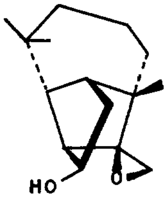
VI: X = Br
VII: X = OH
VIII: X = H



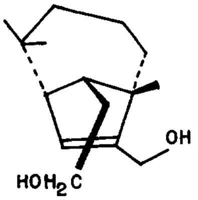
IX: X = Br
X: X = OH



XI: X = Cl
XII: X = OH



XIII



XIV (≡ III)

Alcohol VII, when exposed to one molar equivalent of Cl_2 (5% soln in CCl_4) at 0° (5 min), in presence of Li_2CO_3, was nearly quantitatively converted into the expected chloro aldehyde XI (IR: HC=O, 2705, 1720 cm^{-1}. PMR: tert. Me's 0.93, 0.97, 1.06 ppm; C$\underline{H}_2$Cl, 3.99 ppm, s; C=C$\underline{H}$, 5.94 ppm, br. sig., W_H = 7 Hz; C$\underline{H}$O, 9.70 ppm, t, J = 2Hz). Crude XI on hydrolysis (90% dioxane aq, Li_2CO_3, 40 ± 2°, 10 h) furnished in ~90% yield the hydroxy aldehyde XII (crude; IR: HC=O 2705, 1715 cm^{-1}. PMR: tert. Me's 0.92, 0.97, 1.01 ppm; C$\underline{H}_2$OH, 4.07 ppm, s; C=C$\underline{H}$, 5.73 ppm, br. sig., W_H = 7Hz; C$\underline{H}$O, 9.73 ppm, t, J = 2Hz). $NaBH_4$ reduction (EtOH, 30°, 3 h) of XII, gave in excellent yield, the desired secolongifolene diol XIV (≡ III), m.p. 117° (Et_2O-light pet.), $[\alpha]_D$-23 ± 2° ($\underline{c}$ ≃ 1.06%, $CHCl_3$).

PMR: tert. Me's 0.93, 0.93, 1.03 ppm; $CH_2C\underline{H}_2OH$, 3.57-3.81 ppm, unresolved m; $CHC\underline{H}_2OH$, 4.10 ppm, br. sig., W_H = 4 Hz; $C=C\underline{H}$, 5.74 ppm, unresolved m. For the naturally occurring (+)-seco-longifolene diol, Dorn and Arigoni record[3] m.p. 117°, $[\alpha]_D + 3°$; PMR ($CDCl_3$) : 0.94 (6H), 1.04 (3H), 3.67 (2H), 4.08 (2H), 5.71 (1H) ppm.

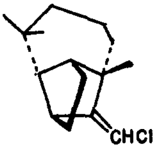
Dorn and Arigoni[3] implicate fragmentation of hydroxy epoxide (XIII mirror image) as an hypothetical precursor in their proposed biosynthesis of (+)-seco-longifolene diol from (–)-longifolene (VIII mirror image). This appears quite plausible in view of facility with which such fragmentations occur under acid-catalysis, as demonstrated earlier[2] for some similarly constituted β-hydroxy-1,2-epoxides. In an attempt to prepare XIII by the action of perbenzoic acid (toluene-benzene soln, -5°, 24 h) on 4-hydroxy-longifolene (VII), the bicyclic aldehyde XII was directly formed, though in a yield of ~ 30%. The extraordinary labile character of XII is understandable in view of the known properties of longifolene epoxide[11].

Satisfactory elemental analysis were obtained for all new compounds.

References and Notes

1. MRC Communication No. 10
2. J.S. Yadav, H.P.S. Chawla and Sukh Dev, Tetrahedron Letters 201 (1977).
3. F. Dorn and D. Arigoni, Experientia **30**, 851 (1974).
4. U.R. Nayak and Sukh Dev, Tetrahedron **24**, 4099 (1968).
5. M. Gaitonde, P.A. Vatakencherry and Sukh Dev, Tetrahedron Letters 2007 (1964).
6. PMR spectra were taken on Perkin-Elmer model R-32 (90 MHz) NMR spectrometer, using CCl_4,except for compounds III and VII, for which $CDCl_3$ was used. IR spectra were recorded as Nujol mull (solids) or as liquid.
7. G. Mehta, U.R. Nayak and Sukh Dev, Tetrahedron **24**, 4105 (1968).
8. See e.g.: G.A. Olah and P. von R. Schleyer (Editors), Carbonium Ions, Vol. III, pp. 1235-1252, 1274-1280, 1295-1341. Wiley-Interscience, New York (1972).

9. (+)-ψ-Longifolol[7] (m.p. 78.5-79.5°; $[\alpha]_D$ + 26.03°, $CHCl_3$) was also prepared in 10-12% yield from (+)-longifolene by chlorination, followed by hydrolysis, the main product of the reaction being the vinyl chloride [**1**: PMR: tert. Me's, 0.95, 0.95, 1.02 ppm; C=CHCl, 5.54 ppm (*trans*), 5.77 ppm (*cis*)].



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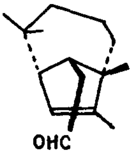
Also see: G. Mehta, S.K. Kapoor and B.G.B. Gupta, *Indian J. Chem.* **14B**, 364 (1976).

10. Extended reaction periods led to significant quantities of **2**, arising from fragmentation of VI (IR: HC=O 2700, 1720. PMR: tert. Me's, 0.99, 1.06, 1.06 ppm; HC=C-Me, 1.65 ppm, t, J = 2Hz; C=CH, 5.50 ppm, br.sig., W_H = 7Hz; CHO, 9.76 ppm, d x d, J_1 = 2Hz, J_2 = 3Hz).



2

11. U.R. Nayak and Sukh Dev, *Tetrahedron* **19**, 2269 (1963); A.P. Joshi, U.R. Nayak and Sukh Dev, *ibid.* **32**, 1423 (1976).