

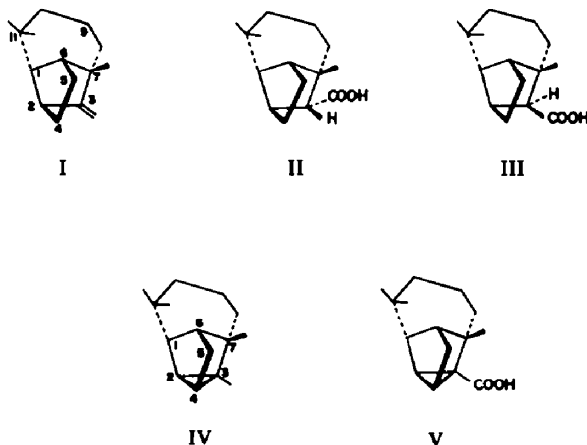
STUDIES IN SESQUITERPENES—XXXVI STRUCTURE OF ψ -LONGIFOLIC ACID*†

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Abstract— ψ -Longifolic acid, a chromic acid oxidation product of longifolene, is unequivocally shown to possess the structure V.

LONGIFOLENE (I), on oxidation under a variety of reaction conditions, is known^{1,2} to give a number of acids, first shown by Naffa and Ourisson³ to be C₁₅-carboxylic acids, derived from I by terminal oxidation. The nature and inter-relationship of these acids was later clarified, when it was shown⁴ that, in all, three C₁₅-carboxylic acids are involved, two of these being represented by II (longifolic acid) and III (isolongifolic acid), while the third, which was named ψ -longifolic acid, was suspected to belong to the longicyclene (IV)⁵ ‡ series. We now present evidence to prove unequivocally that ψ -longifolic acid (m.p. 171–172°) has indeed the longicyclene framework and is represented by V.



The elemental analysis of ψ -longifolic acid⁴ and its derivatives clearly indicates the composition C₁₅H₂₂O₂ (in contrast to C₁₅H₂₄O₂ for longifolic and isolongifolic acids) for the parent acid. The PMR spectrum (Fig. 1) of methyl ψ -longifolate is

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† Abstracted from the Ph.D thesis (Poona University, 1966) of G. Mehta.

‡ Oxidation of camphene with CrO₃-Ac₂O gives, as the acidic product "camphenilanic acid"^{6a} which has been shown to be an epimeric mixture.^{6b}

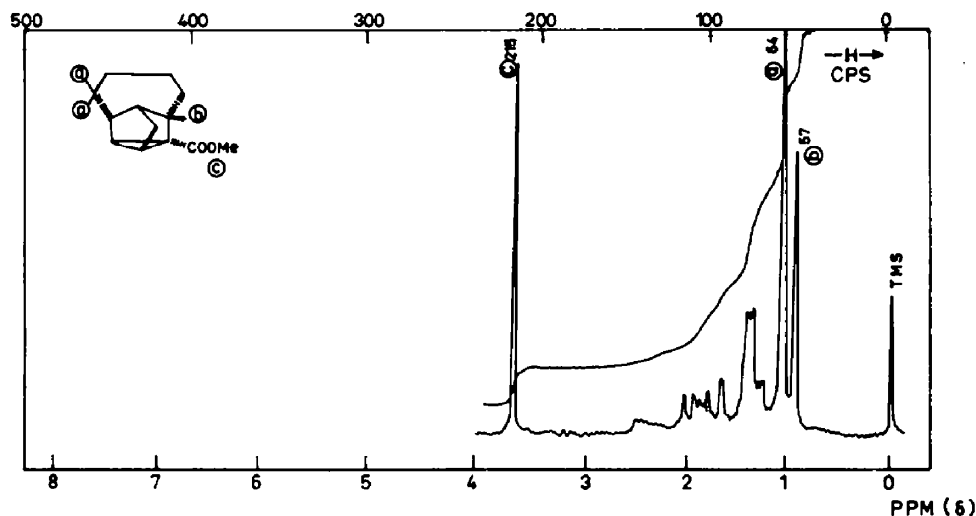


FIG. 1 PMR spectrum of methyl ψ -longifolate.

transparent in the olefinic region. The possibility of occurrence of a tetrasubstituted olefinic linkage in the molecule is clearly ruled out by its end-absorption⁷ in the UV (Table 1). Thus ψ -longifolic acid, being $C_{15}H_{22}O_2$, must be tetracyclic.

TABLE 1. END ABSORPTION IN THE ULTRAVIOLET OF METHYL ψ -LONGIFOLATE AND RELATED COMPOUNDS

	ϵ_{210}	ϵ_{215}	ϵ_{220}	ϵ_{225}
Methyl ψ -longifolate	612	344	238	—
Methyl isolongifolate	98	95	88	—
Longicyclene ⁵	171	113	63	38
Tetrasubstituted olefinic bond ^{7a}	4400–10,000	3900–9200	3400–6700	—

The fourth ring, must have been generated during the oxidation of the tricyclic longifolene to ψ -longifolic acid, and is 3-membered, as is clear from the data. Thus, its methyl ester gives a faint, but distinct yellow colour with tetranitromethane (neat).^{5, 8} Like longicyclene (IV) it shows a band at 3080 cm^{-1} (CCl_4 soln, LiF optics) in the IR, assignable to C—H stretching of the cyclopropane ring;⁹ this absorption is further supported by the presence of its first overtone band in the near IR at $1.627\ \mu$, which is considered diagnostic of tricyclene and quadricyclene types containing cyclopropane ring.^{10, 11} On the basis of these data, the formulation of ψ -longifolic acid as a derivative of longicyclene appeared attractive, the carboxyl function being obviously located at C_3 (V). Full support for this structure was forthcoming from the PMR and UV spectra of methyl ψ -longifolate and its derivatives.

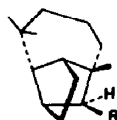
The PMR spectrum of methyl ψ -longifolate (Fig. 1) shows three quaternary

Me's (sharp singlets at 57, 64 and 64 c/s); however, the total number of protons under these peaks amounts to eleven. This may be compared with the same region in the PMR spectrum of longicyclene:⁵ quaternary Me's at 49, 53, 58 and 60 c/s, ~one cyclopropane ring proton at 46 c/s; the total area under these signals being equal to 14 protons. Thus, like longicyclene, two cyclopropane ring methines are indicated under the Me signals; the relative down-field shift of these signals in the ester is in accord with the location of a methoxycarbonyl function (being vicinal to these protons) on the 3-membered ring.

LAH reduction of the methyl ester gave the corresponding alcohol (VIa, m.p. 78–79°. IR spectrum in CCl₄: OH 3640, 3450, 1020 cm⁻¹; cyclopropane 3030 cm⁻¹), the PMR spectrum of which displays an AB quartet (assignable to CH₂OH) centred at 218 c/s with $J_{AB} = 12$ c/s and $J_{AB}/\delta_B - \delta_A = 1.4$. Thus, —CH₂OH (and consequently —COOMe) must be attached to a fully substituted carbon. The alcohol on



VIa: R = CH₂OH
VIb: R = CHO



VIIa: R = CH₂OH
VIIb: R = CHO

pyridine-chromic acid oxidation furnished ψ -longifolal (VIb, IR spectrum: CHO 2730, 1710 cm⁻¹; cyclopropane ring 3090 cm⁻¹). As anticipated, its PMR spectrum (Fig. 2) shows the aldehyde proton as a sharp singlet; this signal occurs at 550 c/s, which is considerably up-field, for example, as compared to the aldehyde proton signal (doublet, $J = 2$ c/s) in isolongifolaldehyde (VIIb), which occurs centred at

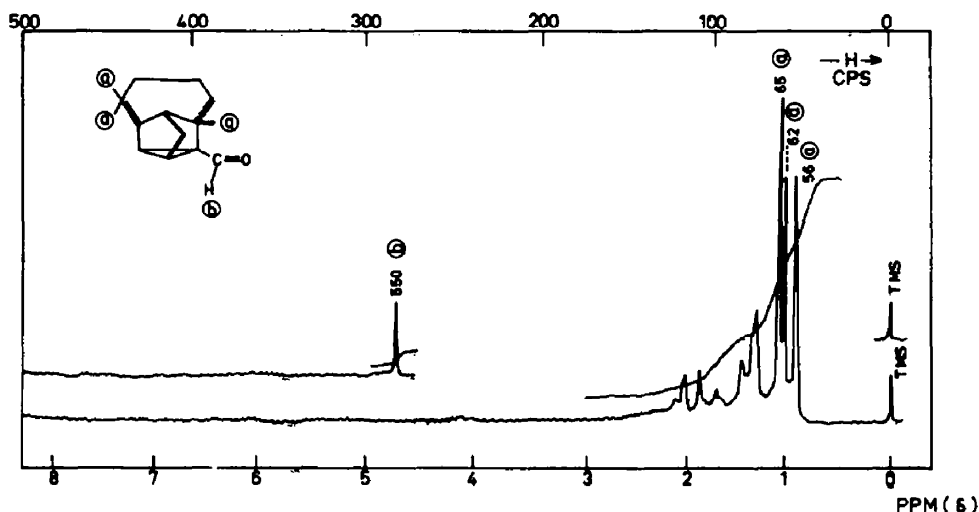
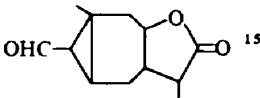


FIG. 2 PMR spectrum of ψ -longifolal.

588 c/s.^{12*} This large shift is fully consonant with the structure VIb for ψ -longifolal, as arising from the diamagnetic shielding of the aldehyde proton by the vicinal anisotropic¹³ cyclopropane ring. Recently, such shielding effects have been encountered in a number of cyclopropane compounds.¹⁴ The UV absorption of the aldehyde (as well as that of its 2,4-dinitrophenylhydrazone) also clearly supports the part structure of a cyclopropane carboxaldehyde in VIb, as it shows the expected cyclopropane-carbonyl conjugation absorption (Table 2); such a chromophore

TABLE 2. UV ABSORPTION OF ψ -LONGIFOLALDEHYDE AND RELATED SUBSTANCES

Compound	Aldehyde		2,4-DNP	
	$\lambda_{\max}^{\text{EtOH}}$ (m μ)	ϵ	$\lambda_{\max}^{\text{EtOH}}$ (m μ)	ϵ
ψ -Longifolal (VIb)	—	$\epsilon_{215} = 4700$	372	25,900
Isolongifolal (VIIb)	—	$\epsilon_{215} = 106$	360	24,700
		$\epsilon_{209} = 4470$	369	26,300

displays λ_{\max} in the range 205–215 m μ with an ϵ value of the order 3000–8000 in a variety of molecular framework¹⁶ and, the corresponding 2,4-DNP shows λ_{\max} around 370 m μ with a high extinction coefficient.¹⁷ The relatively higher end absorption for methyl ψ -longifolate (Table 1) is now understandable in terms of the structure V.

Finally, a direct chemical correlation of V with longicyclene (IV) was undertaken. Our efforts to secure the parent hydrocarbon *via* the reductive detosylation sequence¹⁸ proved abortive, as ψ -longifolal (VIa), under a variety of conditions, failed to give the tosylate.† Next, the NaBH₄ reductive cleavage of the tosylhydrazone²⁰ derived from the ψ -longifolal was undertaken. ψ -Longifolal (VIb) readily yielded the corresponding tosylhydrazone (m.p. 122–123°), which, however, on reaction with NaBH₄ yielded essentially longifolene (I) with only 5% of longicyclene (IV). Though this appears to be the first example of olefin formation during NaBH₄ reduction of tosylhydrazones, olefin formation during such reductions with LAH has been recorded.²¹ The formation of longifolene, in the above reaction, incidentally proves the point of attachment of the carboxyl function in ψ -longifolic acid as in V. Ultimately, Wolff-Kishner reduction of ψ -longifolal semicarbazone, using Henbest's procedure,²² gave a hydrocarbon, identified (GLC, IR, PMR) as the targeted compound, longicyclene (IV).

The above results rigorously define ψ -longifolic acid as V.

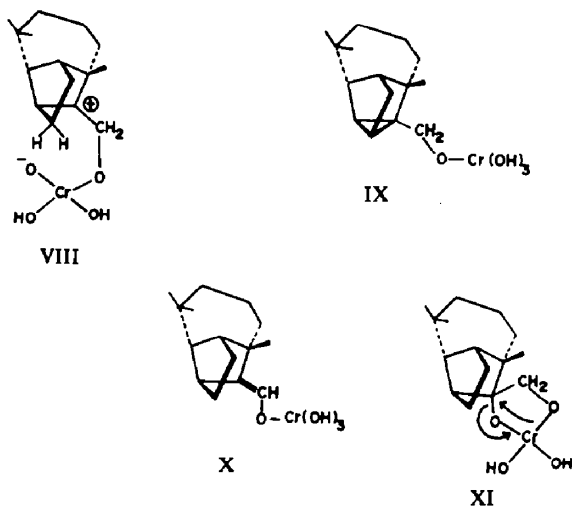
Since, it is conceivable that longifolene employed for oxidation experiments by earlier workers, might have been contaminated with some longicyclene, it was

* Such protons in aliphatic aldehydes occur in the region $\delta = 9.5$ –9.8 ppm.¹²

† Negligible ether-soluble material could be extracted and most of the product was water-soluble.¹⁹

considered desirable to show that ψ -longifolic acid is a genuine product of oxidation of longifolene.* When a rigorously purified sample of longifolene was oxidized with $\text{H}_2\text{CrO}_4\text{-AcOH}$ (containing some H_2SO_4), the acids produced contained 15% ψ -longifolic acid, besides longifolic (10%) and isolongifolic acids (75%).

It is conceivable that the species VIII, arising from the electrophilic attack of Cr^{VI} on the longifolene double bond,† collapses by 1,3-proton elimination (with a concerted proton capture by Cr^{IV} anion;?) to the ψ -longifolol Cr^{IV} derivative (IX) or by 1,2-elimination to the longifolaldehyde enol derivative (X) and these intermediates, next, give rise to the products observed. Alternately, longifolene epoxide, which can arise from VIII (XI is considered less likely, because of steric factors) can be implicated as the intermediate leading to the three acids.‡ §



EXPERIMENTAL

All m.ps and b.ps are uncorrected. Pet. ether refers to the fraction b.p. 40–60°. All solvent extracts were dried over Na_2SO_4 .

IR spectra were taken on a Perkin-Elmer infracord model 137E. UV and NIR spectra were measured on a Perkin-Elmer spectrophotometer, model 350. All PMR spectra were taken in 10–20% soln in CCl_4 with TMS as internal standard, on a Varian Associates A-60 spectrophotometer; peaks are reported in c/s from TMS.

GLC was carried out on a Wilkens Aerograph A-350-B instrument using H_2 as the carrier gas and a 150 cm \times 4.5 mm column packed with 20% diethylene glycol succinate on Chromosorb W (unless otherwise stated).

ψ -Longifolic acid. The acid and the methyl ester were prepared as described previously^{4,||} and had the same characteristics as reported earlier.

* Tricyclene is known to give tricyclenic acid, though in v. poor yields, on such oxidations.²³

† For a recent review of the chromic acid oxidation of alkenes.²⁴

‡ This is considered less likely in view of the fact that whereas perbenzoic acid oxidation of longifolene produces some longifolic and isolongifolic acids, practically no ψ -longifolic acid is formed.²⁵

§ As one of the products of the action of lead tetra-acetate on longifolol, an aldehyde yielding on further oxidation ψ -longifolic acid, has been isolated. (Private communication from Prof. G. Ourisson).

|| Some acid was kindly made available by Dr. J. Lhomme and had been obtained by the method cited²⁶ earlier. The authors wish to record their thanks for the same.

ψ -Longifolol (VIa). Methyl ψ -longifolate (1.03 g) in dry ether (10 ml) was added dropwise (10 min) to a stirred slurry of LAH (0.13 g) in ether (10 ml) at room temp ($\sim 25^\circ$). After stirring for an additional 2 hr, moist ether (20 ml) was cautiously added, followed by aq. Rochelle salt (12 ml, 10%). The reaction mixture, after the usual work up, gave a white solid (0.99 g, m.p. $74-77^\circ$) which was crystallized from acetonitrile to give colorless needles (0.79 g), m.p. $78-79^\circ$, $[\alpha]_D +26.7^\circ$ (c, 1%). PMR spectrum: quaternary Me's 53, 55, 59 c/s. (Found: C, 82.13; H, 11.47. $C_{15}H_{24}O$ requires: C, 81.76; H, 10.98%).

The acetate was prepared by the pyridine- Ac_2O method and had: b.p. $120^\circ/2$ mm, n_D^{30} 1.4915, $[\alpha]_D +18.28^\circ$ (c, 1%). IR spectrum: OAc 1745, 1240 cm^{-1} . PMR spectrum: quaternary Me's 54, 54, 59 c/s; CH_3CO , 3H singlet at 117 c/s; CH_2OAc , 2H singlet at 248 c/s. (Found: C, 77.93; H, 10.32. $C_{17}H_{26}O_2$ requires: C, 77.82; H, 9.99%).

Isolongifolol (VIIa). Methyl isolongifolate⁴ (m.p. $55-56^\circ$, 2.5 g) was reduced with LAH (0.4 g) exactly as described for VIa to give isolongifolol (2.24 g) colourless, short needles (acetonitrile), m.p. $113-114^\circ$, $[\alpha]_D -57.3^\circ$ (c, 0.9%). (Lit.²⁶: m.p. $113-114^\circ$, $[\alpha]_D -53^\circ$). (Found: C, 81.08; H, 12.28. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%).

ψ -Longifolol (VIb). ψ -Longifolol (548 mg) in dry pyridine (5 ml) was added with swirling to a slurry of CrO_3 -pyridine complex²⁷ (661 mg CrO_3 and 6 ml pyridine) at room temp (25°). After 2 hr (under N_2), the reaction mixture was diluted with water (30 ml) and extracted with ether ($40\text{ ml} \times 3$), washed the extract successively with HCl aq (10%; 15 ml $\times 2$), Na_2CO_3 aq. (sat), brine and dried. The solvent was removed and the residue distilled to give VIb as a liquid (516 mg), b.p. $150-160^\circ$ (bath)/3 mm, $[\alpha]_D +23.9^\circ$ (c, 0.9%). PMR spectrum: quaternary Me's 56, 62, 65 c/s. The aldehyde is very susceptible to air oxidation and a satisfactory analysis could not be obtained. Semicarbazone (pyridine method) was readily obtained as a white solid (m.p. $210-212^\circ$), which on crystallization from aqueous EtOH containing a few drops of pyridine was obtained in colorless prisms, m.p. $215-216^\circ$. (Found: N, 15.15; $C_{16}H_{25}ON_3$ requires: N, 15.26%). 2,4-Dinitrophenylhydrazone (HCl method) crystallized in orange silky needles from aqueous ethanol-pyridine, m.p. $197-198^\circ$. (Found: N, 14.06; $C_{21}H_{26}O_4N_4$ requires: N, 14.05%).

Isolongifolol (VIIb). Isolongifolol (522 mg) was oxidized exactly as described for VIb to give the corresponding aldehyde as a colorless oil (490 mg): b.p. $150-160^\circ$ (bath)/3 mm, n_D^{30} 1.5085, $[\alpha]_D +11.1^\circ$ (c, 1.2%). IR spectrum: $HC=O$ 2740, 1730. PMR spectrum: quaternary Me's 58, 61, 64 c/s. A satisfactory elemental analysis could not be obtained. Semicarbazone, colorless micro needles (aqueous methanol-pyridine), m.p. $215-216^\circ$. 2,4-Dinitrophenylhydrazone (HCl method), canary yellow, silky needles (aqueous EtOH), m.p. $157-158^\circ$. (Found: N, 14.34; $C_{21}H_{26}O_4N_4$ requires: N, 14.00%).

$NaBH_4$ reduction of ψ -longifolaldehyde tosylhydrazone: ψ -Longifolaldehyde tosylhydrazone. The aldehyde (253 mg), tosylhydrazine (300 mg) and dry MeOH (15 ml) were refluxed for 4 hr, part of MeOH distilled off and the soln cooled to give a solid (239 mg, m.p. $112-114^\circ$), which was recrystallized from MeOH: colorless, silky needles (186 mg), m.p. $122-123^\circ$. (Found: N, 7.38. $C_{22}H_{30}O_2N_2S$ requires: N, 7.25%).

Reduction with $NaBH_4$. The above tosylhydrazone (111 mg), $NaBH_4$ (246 mg) and dry MeOH (10 ml) were refluxed for 10 hr. The reaction mixture was cooled, diluted with water and extracted with ether ($25\text{ ml} \times 3$). The extract was washed with brine (15 ml $\times 2$), $NaHCO_3$ aq and again with brine (15 ml $\times 2$), and dried. The solvent was removed and the product (oil, 56 mg), filtered in hexane soln through a small column of silica gel (grade IIA, $10\text{ cm} \times 1\text{ cm}$) to give a colorless oil (22 mg). GLC analysis (temp 130° , flow rate 50 ml/min) showed it to consist of longifolene (95%, RRT 1.61) and longicyclene (5%, RRT = 1); this composition was confirmed by IR spectrophotometry.

Wolff-Kishner reduction of ψ -longifolaldehyde semicarbazone. The semicarbazone (m.p. $215-216^\circ$, 374 mg) in dry toluene (15 ml) was dried by distilling off some solvent (5 ml). To this freshly sublimed $KOBu'$ (260 mg) was introduced and the mixture refluxed for 36 hr. The reaction mixture was poured into water (25 ml), the toluene layer separated, the aqueous portion extracted with pet. ether ($30\text{ ml} \times 3$) and the combined organic phases successively washed with HCl aq (10%), saturated Na_2CO_3 aq and brine and dried. Solvent was removed to get an oil (206 mg) which was filtered through silica gel (grade IIA, $10\text{ cm} \times 1\text{ cm}$) in hexane. The product was distilled to get a colorless oil (151 mg): b.p. $100-110^\circ$ (bath)/2 mm, n_D^{30} 1.4913, $[\alpha]_D +31.9^\circ$ (c, 0.7%). GLC showed only one component corresponding to longicyclene.

Chromic acid oxidation of GLC pure longifolene. To a stirred soln of GLC pure longifolene (5 g) in gl AcOH (25 ml) was added dropwise a soln of Cr_2O_6 (10 g) in water (8 ml) and conc H_2SO_4 (0.3 ml), the temp being maintained $\sim 45^\circ$ by external cooling. After the addition was complete (30 min) the reaction mixture was worked up by diluting with water (100 ml), extraction by ether ($100\text{ ml} \times 3$) and separating the acid portion by extraction with 10% KOH aq ($50\text{ ml} \times 3$). Acidification of the aqueous phase with HCl aq extraction with ether followed by washing with brine and solvent removal yielded a yellowish

gummy solid (1.8 g). Esterification of the acid in ether with CH_2N_2 , followed by distillation furnished the esters mixture as a pale yellow oil: b.p. 134–137°/5 mm (1.71 g). GLC analysis (Column; 20% silicone-SE 30 on Chromosorb W; temp 180°; flow rate 70 ml/min) indicated: longifolic acid (10%, RRT = 1), ψ -longifolic acid (15%, RRT = 1.104) and isolongifolic acid (75%, RRT = 1.208).

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