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STUDIES IN SESQUITERPENES—LV†‡

ISOLONGIFOLENE(PART 6)§: MECHANISM OF REARRANGEMENT OF LONGIFOLENE TO ISOLONGIFOLENE-I#

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Abstract—The gross mechanism of rearrangement of longifolene to isolongifolene has been elucidated by using site-specifically labelled longifolene-4, 4, 5, 5-d_4 and shown to follow the pathway proposed by Berson *et al.*, which involves an *exo, exo* Me shift, in preference to the *endo, endo* Me migration route proposed earlier. An efficient synthesis of longifolene-4, 4, 5, 5-d_4, the key compound in the present investigation, is described.

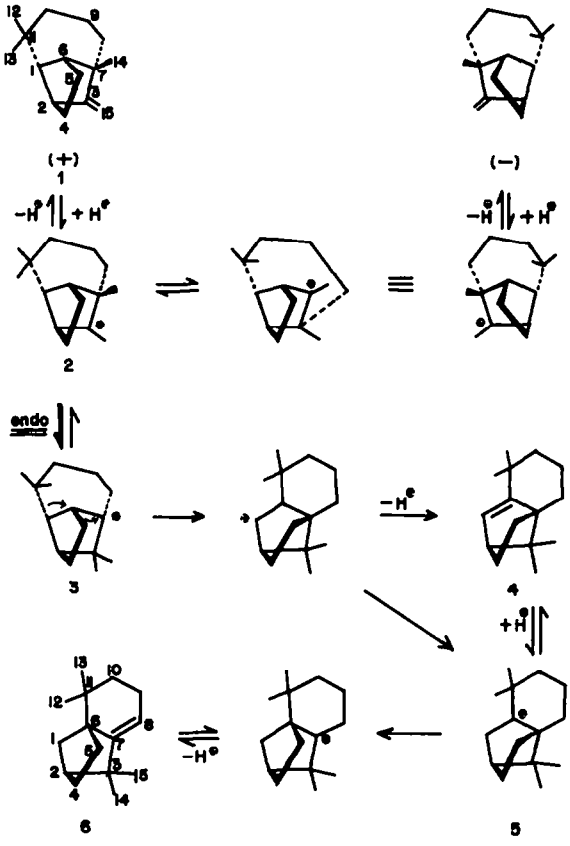
(+)-Longifolene (**1**), the major sesquiterpens of Indian turpentine oil (ex *Pinus longifolia* Roxb.), on exposure to strong protic or Lewis acids, undergoes a deep-seated molecular rearrangement to an isomeric tricyclic hydrocarbon, (−)-isolongifolene (**6**), structure of which has been established unequivocally by degradation[1,2] and synthesis.[3] It was also established that isolongifolene, thus obtained, is racemized to varying degrees.[1] A mechanism (*Scheme* 1) was proposed[1,4] to rationalize these results; it may be noted that in this scheme, in going from ion **2** to **3**, an *endo, endo* Me migration is involved. Subsequently, Berson *et al.*,[5] based on their extensive studies of methyl norbornyl cations, pointed out that such *endo* migrations are energetically unfavourable and proposed a modified pathway (*Scheme* 2), wherein the much more precedented *exo, exo* (**9** to **10**) shift occurs. Still later, McMurry[6] suggested the intermediacy of longicyclene[7] (**11**), in order to evolve a simplified version of Scheme 2 (Scheme 3)

In this and the following communication we describe work designed to distinguish between these alternatives.

STRATEGY AND RESULTS

It is important to distinguish between Scheme 1 and Scheme 2 first, as Scheme 3 raises the general question of possible intermediates, which may lie on the reaction pathway and this is best dealt with after obtaining an answer to the first question.

A perusal of the two schemes will rapidly reveal that it is not possible to distinguish between these



Scheme 1.

alternatives by ordinary methods such as that of configurational correlation, as both pathways result in the same enantiomer of isolongifolene. This has been briefly commented on by Berson *et al.*,[5] who suggested a solution based on rearrangement of C(1), C(11)-carbon-labelled longifolene. While looking for a simpler solution, it became obvious that if one subjects longifolene-4, 4, 5, 5-d_4 (**12**) to this rearrangement, the two routes would lead to

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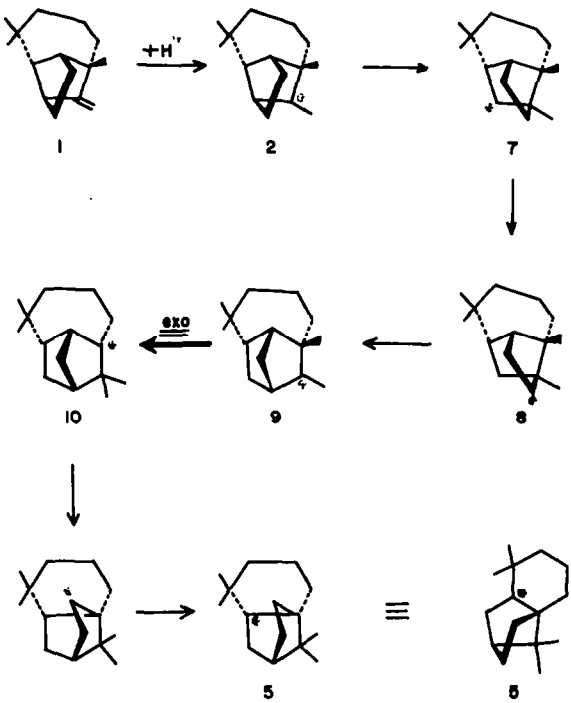
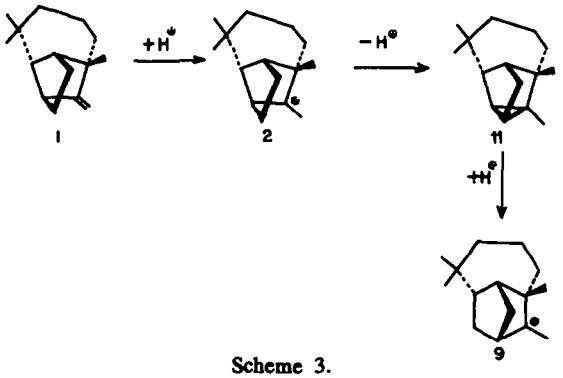


Scheme 2.

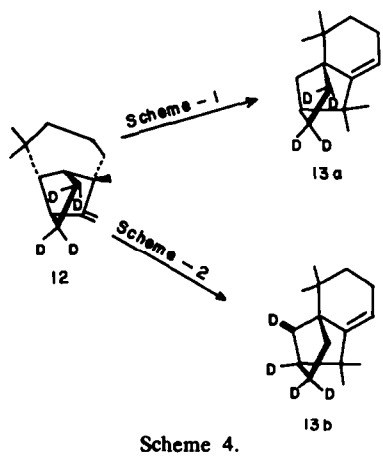


Scheme 3.

isolongifolene-d_4 having different deuterium substitution patterns (Scheme 4), which should be easily discernible. In view of this, synthesis of **12** was undertaken.

Synthesis of Longifolene-4, 4, 5, 5-d_4 (**12**): Any method for introducing deuterium at C(4) and C(5) in longifolene would first require suitable functionalisation, such as introduction of a CO group, at either of these positions in longifolene. It has been reported[8,9] that 3-isolongifololt (**14**) on lead tetraacetate oxidation gives ether **15**, which appeared to be suitable for further elaboration into

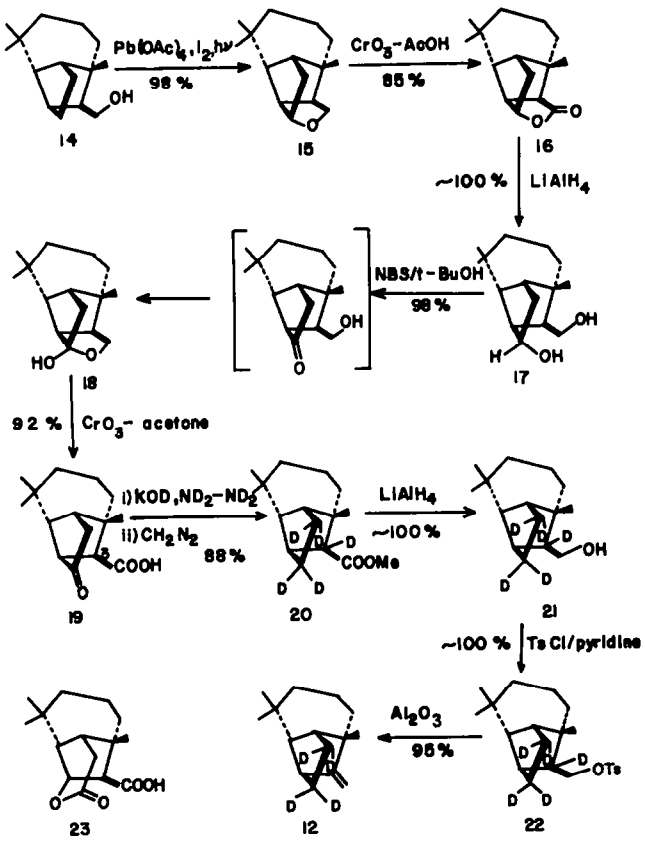
† Compounds with C(3) *endo* (with respect to the bicyclo [2. 2. 1] heptane system) configuration, in longifolene chemistry, invariably carry the prefix iso, e.g. isolongifolic acid,[14] isolongifolol,[8] etc. Since these compounds have the longifolene carbon skeleton (**1**) and *not* that of isolongifolene (**6**), this nomenclature tends to be confusing. It is suggested that such compounds of the longifolene series should carry the *prefix* 3-iso, instead of only iso to distinguish them from compounds based on isolongifolene skeleton.



Scheme 4.

the required longifolene-d_4. The first prerequisite, however, was to obtain ether **15** in more satisfactory yields, as both groups of previous workers had isolated **15** in yields of 20–30% only, the major product being acetate of **14**. We have now succeeded in getting almost quantitative yields of this ether by a procedure described in detail under the 'Experimental Part'; the major reasons for this dramatic improvement in the yield appear to be the use of $Pb(OAc)_4$/Iodine/$h\nu$[10] rather than $Pb(OAc)_4$ alone and, the innovative use of silica gel impregnated with potassium iodide, which greatly facilitated work-up. Scheme 5 outlines various steps employed for the elaboration of **15** into the required **12**. Some comments appear to be in order.

The known[8,9] oxidation of ether **5** to the γ-lactone (**16**) with CrO_3/AcOH proceeded smoothly.[11] In the first instance, direct oxidation of diol **17** to the keto acid **19** with CrO_3/H_2SO_4 in acetone, was investigated. Though, this conversion could be effected, yields were unsatisfactory (~ 50%) and further oxidation to the lactone acid **23** occurred.[12] The two-stage oxidation, as outlined in Scheme 5 and, which is based on selective oxidation of secondary hydroxyl in **17** with NBS[13], proved most satisfactory. The next transformation *viz* **19**→**20**, which is crucial to our purpose, could be most conveniently carried out by Wolff-Kishner reduction, using KOD, $ND_2{\cdot}ND_2{\cdot}D_2O$ and diethylene glycol-O-d_2. The product (as Me ester) showed by mass spectrometry, an average deuterium content of 4.34 D/molecule (Rel. % deuterated species: D_3, 8; D_4, 49; D_5, 43) and by glc,[14] consisted of 95% of **20** and 5% of its less stable C(3) epimer; the extra deuterium is principally due to the anticipated incorporation at C-3, which is borne out by the last elimination product (**12**), and some random incorporation.[15] LAH reduction of **20** gave 3-isolongifolol-d_5. 3-Isolongifolol (**14**) has been previously converted into longifolene with PCl_5/ether, but in poor yields.[16] It has also been mentioned,[17] in passing, that 3-isolongifolyl tosylate[18] on solvolysis yields longifolene, but in an unspecified yield. Since, this step is critical for final yields, we have investigated elimination of 3-isolongifolyl tosylate and find that excellent conversions occurs on exposure to Al_2O_3.[19,20] This method was finally employed to get

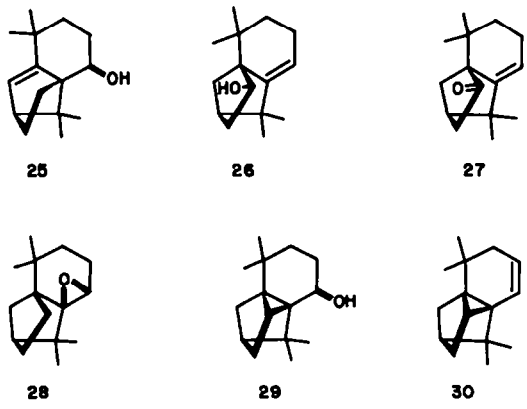


Scheme 5.

an excellent yield of the targeted compound **12**, having an average deuterium content of 3.5 D/molecule (Table 1).

Isomerization to isolongifolene-d_4 and location of deuterium label. Exposure of **12** to BF_3·Et_2O[1] gave isolongifolene-d_4, in which the deuterium atoms must now be located unequivocally in order to distinguish between the alternatives **13a** and **13b**, From the known chemistry of isolongifolene, compounds **25**,[21,22] **26** and **27**[23] appeared most appropriate for the purpose, as each one of these is eminently suitable for spectroscopic distinction between the two deuterium distribution possibilities (Table 1).

Preparation of **25** from isolongifolene epoxide **28**[22] had already been standardised by us earlier.[21] It has been reported[23] that cycloisolongifolol[21] (**29**) on exposure (25°) to aqueous phosphoric acid gives, in good yield, alcohol **26**. However, in our hands only poor yields (~10%)† of this compound could be obtained, the major product being the olefin **30**.[21] Subsequently, we found that rearrangement of cyclopropyl carbinol **29** to the required homoallylic alcohol **16** was best carried out with $AcOH/H_2SO_4$, when the acetate of **26** could be



25 **26** **27**

28 **29** **30**

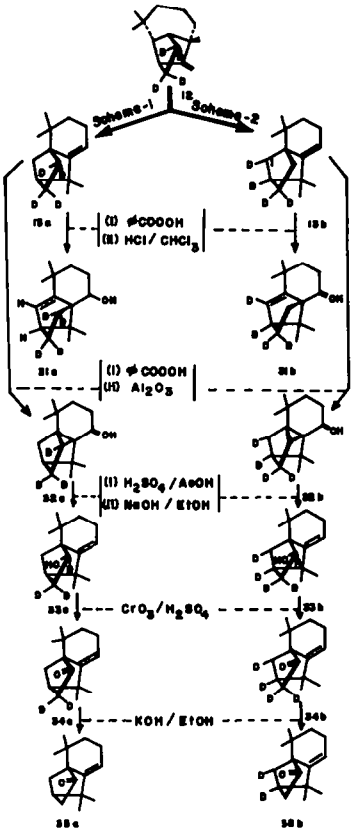
easily obtained in over 50% yield. Oxidation of **26** to **27** with CrO_3/H_2SO_4 in acetone proved straightforward.

These reactions, when applied to isolongifolene-d_4, furnished the required compounds **31**, **33**, **34** (Table 1) for further spectral scrutiny.

The rearranged secondary alcohol **25**, in its PMR spectrum, shows, as expected, the olefinic proton signal as a doublet (5.70 ppm, J = 3.5 Hz).[21] On the other hand, the deuterated compound (Table 1) displays, in its PMR spectrum, this signal with much reduced intensity (0.25 H) and as a *singlet*. This clearly supports structure **31b**, as in going

†In a private communication from Dr. G. W. Shaffer, we were later informed that original yields could not be reproduced and average yields were of the order of 10-15%. We are grateful to Dr. Shaffer for this information, as well as for an authentic sample of **26**

Table 1. Expected and found D in various derivatives from Isolongifolene-d_4)

Reactions conducted and expected D – pattern of the products	D Found: Rel. % deuterated species D_0	D_1	D_2	D_3	D_4	D_5	Total D/ molecule
	0	1	7	35	49	8	3·56
	0	3	14	29	43	11	3·45
	0	3	10	26	50	11	3·56
	1	2	9	24	52	12	3·60
	0	2	8	23	54	13	3·68
	1	2	9	25	54	9	3·56
	8	13	45	30	4	0	2·09

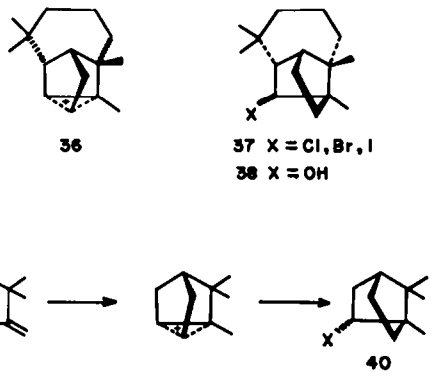
from **13b** to **31b** *via* the epoxide, C(1) proton, which has approximately antiperiplanar geometry with respect to the developing vacant orbital in the transition state for the rearrangement, will be preferentially lost, and C(2) now has deuterium.

Alcohol **26** shows CHOH signal at 3.80 ppm (dd, $J_1 = 3$Hz, $J_2 = 6$ Hz, 1H) in its PMR spectrum. The corresponding deuterated derivative (Table 1) also shows a 1H signal at 3.80 ppm, (but as a singlet) and this dictates its formulation as **33b** and not **33a**. As expected, the derived ketone **34b** still has all the deuterium in tact; if **34a** were the structure, 50% of the deuterium should have been lost. On exposure to KOH/EtOH (10%, 16h, reflux), ketone **34b** lost 41% of its deuterium (Table 1); though the loss expected was 50%, it is known[24] that in bicyclo [2. 2. 1] heptan-2-ones, such as **34b**, the *endo* proton (deuterium) is somewhat resistant to replacement.

The above results clearly rule out the mechanism depicted in Scheme 1 and provide full support, for the gross features of the alternative pathway (Scheme2) proposed by Berson *et al.*

DISCUSSION

A strong preference for *exo, exo* 3,2-hydride/Me migration for bicyclo [2.2.1] heptane system, in general, is now well established,[25,26] though at least two cases of *endo, endo* migration, arising from certain special structural features, have been recorded.[27,28] However, the theoretical basis for this preference is still a subject of controversy.[25a] The most widely advanced[25b] explanation for this stereospecificity, advocated initially by Berson,[5] rests on the intermediacy of non-classical ion, a concept which has been under active investigation and considerable controversy during the past several years.[24] However, in longifolene chemistry, the bridged ion such as **36** is considered unimportant,[4] since the addition of hydrogen halides to longifolene results in longibornyl halides **37** and not longiisobornyl halide, expected on analogy with the reactions of comphene (**39**, **40**); hydration[30] also results in substitution from the *endo* face giving longiborneol (**38**). In analogy with this stereochemical outcome from reactions involving external nucleophiles, one would have expected, at least, some participation of the *endo*-migration route (Scheme 1) to-wards isolongifolene development. However, from the deuterium incorporation data (Table 1) it is amply clear that this is not so. While looking for a suitable rationale for why the more circuitous route (Scheme 2) to the ion **5** is completely preferred over the more direct route (Scheme 1), another



important factor became apparent. In our proposal (Scheme 1), methyl migration leads to ion **3**, in which charge is located at the bridgehead of bicyclo [4.2.1] nonane part of the system, while on the otherhand, in the corresponding ion **10** of Scheme 2, the charge is on the bridgehead of bicyclo [4.3.1] decane system, which as can be seen from a study of molecular models (Dreiding), can easily accommodate a planar triagonal carbon at the bridgehead in sharp contrast to **3**, where the bicyclo [2.2.1] heptane system must be severely distorted to do this. Thus, ion **3** should be less stable relative to **10** and this energy difference may provide additional barrier to the pathway depicted in Scheme 1. It is true that bridgehead carbonium ions on bicyclo [3.2.1] octane systems have been invoked to account for certain rearrangements in the caryophyllene[31] and thujopsene[32] series, in our present consideration of the ions **3** and **10**, we are concerned with the thermodynamic energy difference.

EXPERIMENTAL

Petroleum ether refers to fraction b.p. 40-60°. All solvent extracts were finally washed with brine and dried over $NaSO_4$. Alumina (−100, +250 mesh) was repeatedly washed with boiling water till washings were neutral (phenolphthalein) and then activated at 450° for 6 hr, before use for detosylation and rearrangement reactions.

M.ps were determined in open capillaries and all m.ps and b.ps are uncorrected. Optical rotations were measured in $CHCl_3$. IR spectra were recorded on smears (liquids) or Nujol mulls (solids) unless stated to the contrary, on Perkin-Elmer Infracord model 137 E. ^{1}H-NMR spectra were measured in 10-20% CCl_4 soln, unless otherwise stated, on Varian A-60 or T-60 spectrometer, using TMS as internal standard ($\delta = 0$ ppm); abbreviations used to denote multiplicity are: *s* = singlet, *d* = doublet, *t* = triplet, *q* = quartet, *m* = multiplet, *b* = broad. Mass spectra (MS) were obtained with a CEC spectrometer model 21-110 B, using an ionizing voltage of 70 eV and a direct inlet system; besides the molecular ion, nine most abundant ions are given with their relative intensities. Total deuterium and polydeuterium distribution assays were carried out by mass spectrometry.[33] Natural abundance spectra were also recorded for comparison with spectra of deuterated samples.

Analytical glc was carried out on Aerograph model A-350-B using 150 cm × 0.6 cm aluminium columns packed with 20% diethyleneglycol polysuccinate (DEGS.)/ Silicone SE 30 on Chromosorb W (60-80 mesh) with H_2 as carrier gas. Progress of most reactions was checked by tlc on 0.2 mm layers of silica gel containing 15% gypsum, with visualization with H_2SO_4 spray followed by heating to 120–130°.

4,15-*Epoxylongifolane* (**15**). A mixture of 3-isolongifolol[8] (m.p. 112.5-113°; 20.0 g, 0.09 mole), lead tetraacetate (44.4 g, 0.1 mole) and iodine (11.42 g, 0.09 g, atom) in 250 ml dry, benzene-free cyclohexane, was stirred and refluxed under irradiation from a 250 Watts tungsten lamp, in N_2 atmosphere. At the end of the reaction (0.5 h; tlc: benzene), excess lead tetraacetate was destroyed by the addition of ethanediol (10 ml). To remove free iodine, 35 g of silica gel containing 15% KI (A soln of 30 g KI in water 30 ml, and acetone 400 ml was added to 100–200 mesh silica gel, 170 g, and well mixed by shaking. Acetone and water were removed at 100°/70 mm in a rotary evaporator and the product dried at 120–125° for 3 hr, before use) was added portionwise and stirred for 15 min, when the original dark violet-coloured mixture turned into light pink and the insoluble lead salts became granular. The whole thing was filtered through a bed (5 cm × 4 cm) of grade III alumina/sodium thiosulphate (10:1, w/w) and the bed washed with ether/cyclohexane (1:3, 25 ml × 5). The soln was freed of the solvent and the residue (21 g) distilled to leave **15** as a colourless oil, b.p. 128–130°/2.5 mm, yield 19.0 g; $[\alpha]_D = -37.69$ ($c = 4.8$)-glc: single peak. IR: 1062, 1042, 990, 935. ^{1}H-NMR: 0.93 (*s*, 3H); 0.98 (*s*, 6H); 3.53 (ABX *m*, $J_{AB} = 8.5$ Hz, $J_{AX} = 3.5$ Hz, $J_{BX} = 0$, 2H, OCH_2); 4.18 (*t* × *d*, J = 6 Hz and 1.5 Hz, 1H, OCH).

3-*Isolongifolene*-3,4-*carbolactone* (**16**). A soln of CrO_3 (21 g) in water (40 ml) and AcOH (360 ml) was added, with stirring, to a soln of **15** (19 g) in glacial AcOH (400 ml), and the mixture maintained at 50 ± 2° for 6 hr. The mixture was cooled to 30°, diluted with water (2000 ml) and the product taken up in petroleum ether (500 ml × 4). The extract was washed with water (400 ml), 5% Na_2CO_3 aq (400 ml × 3) and water (300 ml × 2), and dried. The solvent was flashed off and the residue (20 g, m.p. 40–50°) saponified by refluxing with KOH (15 g) in water (10 ml) and MeOH (40 ml), for 3 hr. It was worked up with petroleum ether, in the usual fashion, to give unchanged **15** (1.9 g) and an aqueous alkaline soln, which on acidification with 4N HCl, followed by extraction with petroleum ether (50 ml × 6), washing with 5% Na_2CO_3 aq (50 ml × 3), water (50 ml × 3) and drying gave, after solvent removal, the required lactone **16** (17.0 g), m.p. 52–59°. Recrystallisation from petroleum ether furnished pure **16** (15.0 g), m.p. 60.5-61.5° (lit.[8]: m.p. 60-61°); $[\alpha]_D = +38.68°$ ($c = 5.4$). IR: 1775 (C=O), 1182, 1052, 1038, 1028. ^{1}H-NMR: 1.02 (*s*, 6H); 1.10 (*s*, 3H); 3.07 (*t*, J = 5 Hz, 1H, CHCOO); 4.60 (*t*, J = 6 Hz, 1H, CHOCO).

3-*Isolongifolane*-4(endo), 15-*diol* (**17**). The above lactone (16.0 g) in dry ether (150 ml) was reduced with LAH (3.2 g) in ether (100 ml), in the usual manner (tlc, monitoring: solvent, benzene EtOAc 9:1), to furnish, after work-up with 15% NaOH aq (3.5 ml), the required diol (16.2 g), m.p. 72–78°. This was recrystallised from petroleum ether to give white crystals of **17**, 14.8 g, m.p. 94.5–95.5° (Lit.[8]: m.p. 88–89°): $[\alpha]_D = -46.38°$ ($c = 4.6$). IR: 3250, 1098, 1065, 1040, 1018, 1005. ^{1}H-NMR: 0.93 (*bs*, 9H): 3.40–4.38 (overlapping *m*, 3H, CHOH, CH_2OH).

4-*Hydroxy*-4,15-*epoxylongifolane* (**18**). To a soln of the diol **17** (5.8 g, 0.0243 mole) in t-BuOH (135 ml) containing pyridine (4.5 ml) and water (15 ml), N-bromosuccinimide (8.8 g, 0.0494 mole) was added, in one lot, with stirring at room temp (25–28°). After 0.5 hr (tlc: benzene/EtOAc 9:1), the mixture was diluted with sat $NaCO_3$ aq (150 ml), the product taken up in ether (50 ml × 5) and the extract washed with water and dried. The solvent was flashed off to give **18** (5.8 g) m.p. 122–128°, which was used as such in the next oxidation step.

An analytical sample of **18** was obtained by recrystallisation from petroleum ether, m.p. 133.5–134.5°; $[\alpha]_D =$

+19.05° ($c = 4.2$). IR: no C=O absorption; 1160, 1130, 1118, 1043. ^{1}H-NMR. ($CDCl_3$):0.98 (*s*, 6H); 1.02 (*s*, 3H); 3.70 (ABX *m*, $J_{AB} = 9$ Hz, $J_{AX} = 3$ Hz, $J_{BX} = 0$ Hz, 2H, OCH_2). MS: *m/e* 236 (M^+, 100%), 165 (43), 153 (80), 152 (65), 121 (33), 107 (90), 105 (40), 95 (42), 93 (46), 91 (46). (Found: C, 76.07; H, 9.93. $C_{15}H_{24}O_2$ requires C, 76.22; H, 10.24%).

4-Oxo-3-isolongifolic acid (**19**). (a) A soln of the above crude **18** (5.6 g) in acetone (150 ml) was cooled to 0° and treated, with stirring, with Jones' reagent (12 ml; 6.68 g CrO_3, 5.75 ml conc H_2SO_4 and, diluted to 25 ml with water) and the mixture left aside at 25° for 1 hr. After diluting with water (400 ml), the product was extracted with EtOAc benzene 1:1 (150 ml×4), the extract washed with water and dried. The solvent was removed to give a product (5.3 g, m.p. 170–178°), which was recrystallised from acetonitrile to get pure **19** (5.0 g), m.p. 184–185° (Lit.[8]: m.p. 185–186°). Methyl ester (diazomethane method), crystallised from petroleum ether, m.p. 77.5–78.5° (Lit.[8]: m.p. 68–69°); $[\alpha]_D = +114.5°$ ($c = 5.2$). IR: 1740 (C=O), 1185, 1100. ^{1}H-NMR: 0.97 (*s* 3H); 1.01 (*s*, 3H); 1.08 (*s*, 3H); 3.13 (*d*, J = 5 Hz, 1H, $CHCOOCH_3$); 3.63 (*s*, 3H, $COOCH_3$).

(b) Diol **17** (12.07 g) in acetone (250 ml) was stirred and treated, dropwise, with Jones' reagent, at 0.5°, till an orange colour persisted. After leaving aside at 25° for 1 hr, the mixture was worked up with EtOAc (300 ml×4), in the usual manner and, the extract separated with 10% KOH aq into acid (8.0 g) and neutral (4.1 g) fractions. The acid part showed on tlc (AcOH/EtOAc/benzene 1:5:20) two major components. The crude acid was crystallised from acetonitrile (16 ml) to yield 5 g of **19** (m.p. 184–185.5°), and the mother liquor chromatographed on silica gel (grade III[34], 35 cm×7 cm). Elution with EtOAc/benzene 1:1 (200 ml×4) gave another 1.8 g of **19**, while EtOAc (500 ml) eluted 0.6 g of *lactone acid* **23**, m.p. 221–222° (acetonitrile), which was converted into its *methyl ester*, m.p. 107–108° (petroleum ether); $[\alpha]_D = +19.29°$ ($c = 3.6$). IR: 1740 (C=O), 1200, 1167, 1052. ^{1}H-NMR: 1.07 (*s*, 3H); 1.10 (*s*, 3H); 1.18 (*s*, 3H); 3.0 (*d*, J = 4 Hz, 1H, $CHCOOCH_3$); 3.67 (*s*, 3H, $COOCH_3$); 4.77 (*bd*, J = 4 Hz, 1H, $CHOCO$). MS: *m/e* 280 (M^+, 33%), 237 (44), 205 (25), 137 (95), 136 (100), 135 (31), 121 (55), 109 (73), 107 (51), 105 (50) (Found: C, 68.77; H, 8.69%. $C_{16}H_{24}O_4$ requires: C, 68.54; H, 8.63%).

Methyl 3-isolongifolate -3, 4, 4, 5, 5-d_5 (**20**). To a soln of **19** (4.9 g) in diethylene glycol-O-d_2 (30 ml), KOD in D_2O containing some tertiary butanol-O-d, (prepared by adding 15 ml D_2O to 6.4 g -BuOK) was added, the mixture refluxed for 0.5 hr and then distilled (130–140°/80 Torr.) to remove D_2O, BuOD, etc. To the residue $D_2N{\cdot}ND_2{\cdot}D_2O$ (3 ml) was added and the mixture refluxed for 2 hr and then distilled till the temp of the mixture reached 190–200°, when distillation was stopped and refluxing continued for a further 4 hr period. The mixture was diluted with water (100 ml), and extracted with ether/benzene 1:1 (50 ml×4) to remove unwanted neutral products. The aqueous alkaline portion was acidified (Congo red) with 4N HCl and the product taken up in ether/benzene 1:1 (50 ml×4) and freed of solvent to give the crude acid (4.6 g, m.p. 125–130°) which was esterified with diazomethane to finally yield **20** (4.2 g), b.p. 128–130°/1.5 mm, m.p. 39–45°; glc (SE 30, 120°, 70 ml H_2/min): 95% **20**, 5% C(3) epimer.

3-Isolongifolol-3, 4, 4, 5, 5-d_5 (**21**). The above ester (9.0 g) in dry ether (150 ml) was reduced with LAH (2.6 g) in ether (120 ml), in the usual manner. After the usual work-up with 15% NaOH aq, the required **21** was obtained, which was crystallised from petroleum ether, m.p. 112.5-113.5°, yield = 7.4 g.

Longifolene (**1**) *from 3-isolongifolol* (**14**). 3-Isolongifolol (2.5 g) in pyridine (30 ml) was cooled to 0° and, *p*-toluenesulphonyl chloride (4 g) added in one lot. After 1 hr at 5°, and 12 hr at 25°, the mixture was diluted with ice + water (200 g), the solid collected by filtration, washed with ice-water and dried over P_2O_5 to furnish *3-isolongifolyl tosylate* (4.8 g), m.p. 68–69° (Lit.[18]: m.p. 68–69°). IR: 1580, 1180, 1097, 948.^{1}H-NMR: 0.77 (*s*, 3H); 0.93 (*s*, 3H); 0.97 (*s*, 3H); 2.45 (*s*, 3H); 4.08 (*d*, J = 7 Hz, 2H, CH_2OTs); 7.53 (*q*, J = 8 Hz, 4 aromat. H).

This tosylate (3.6 g) in petroleum ether (100 ml) was loaded on a dry-packed column (20 cm×4 cm) of alumina and left for 12 hr, after which the product was eluted with petroleum ether (350 ml). Removal of solvent, followed by distillation yielded longifolene (2 g), b.p. 95–96°/2.5 mm; glc (DEGS, 90°, 70 ml H_2/min): 90% **1** and 9% isolongifolene.

Longifolene-4, 4, 5, 5-d_4 (**12**). Exactly as detailed above, **21** (4 g) yielded 7.2 g of **22**, m.p. 67–69°, which on exposure to alumina (30 cm×4 cm) furnished **12**, 3.5 g, b.p. 95-96°/2.5 mm; $[\alpha]_D = +48.40$ ($c = 3.3$).

Isolongifolene-1, 2, 4, 4,-d_4 (**13b**). A soln of **12** (8.5 g) in dry benzene (30 ml) containing 0.3 ml $BF_3.Et_2O$, was kept at 23° for 2 hr, and then diluted with 5% Na_2CO_3 aq (20 ml). Usual work up furnished **13b**, yield = 8.1 g, b.p. 94–95°/3 mm; $[\alpha]_D = -80.44°$ ($c = 2.76$).

7,8-Epoxy-isolongifolane-1, 2, 4, 4-d_4. **13b** (7.1 g) in benzene (15 ml) was exposed (5–8°, 6 h) to perbenzoic acid (5 g) in benzene (95 ml) in a manner, already reported[1] for natural abundance isolongifolene, and likewise worked up to furnish the desired epoxide, m.p. 38–41° (n-hexane), yield = 3.6 g.

Rearrangement of 7,8-epoxy-isolongifolane-1, 2, 4, 4-d_4 *to alcohol* (**31b**). The above epoxide (0.5 g) was treated with a $CHCl_3$ soln of dry HCl (0.5%, 5 ml) at −11±1°, exactly as described[21] for **28** and, then, processed the same way to obtain **31b**, m.p. 122–123°, yield = 30 mg.

8-Hydroxy-cycloisolongifolane-1, 2, 4, 4-d_4 (**32b**). Working with natural abundance isolongifolene epoxide (**28**), a procedure, much more efficient than the one reported earlier[21] for the conversion of **28** into **29**, was first worked out and then, applied to isolongifolene epoxide- d_4.

Isolongifolene epoxide-1, 2, 4, 4-d_4 (2.14 g, m.p. 39–41°) in hexane (15 ml) was loaded on a dry-packed column (34 cm×2 cm) of alumina (grade I[35], 100 g) and immediately eluted with benzene/EtOAc 1:1 (250 ml) to furnish, after solvent removal, a crystalline product (2.06 g, m.p. 60–70°), which was recrystallised from acetonitrile to give pure **32b** (970 mg), m.p. 95–96°.

Action of acetic acid/sulphuric acid on cycloisolongifolol (**29**). To AcOH (3 ml) containing 0.05 ml 50% (v/v) H_2SO_4 aq, maintained at 8–10°, cycloisolongifolol (528 mg) was added and the light pink soln left aside at the same temp till practically all of **29** had reacted (tlc: benzene/EtOAc 95:5; 12 h). The mixture was diluted with water (50 ml), the product taken up in hexane (50 ml×4) and the extract washed with water, 5% $NaHCO_3$ aq (50 ml×2), water and dried. The solvent was flashed off to give a product (530 mg), which on programmed glc (DEGS, 120–190°, 110 ml of H_2/min), showed the following composition (increasing retention time): **30** (34%), acetate of **29** (0.5%), acetate of **26** (54%), **26** (4.5%), **29** (7%). This product was chromatographed on silica gel (grade II; 32 cm×1.5 cm) with tlc monitoring.

Frac. 1 (petroleum ether, 50 ml×3; 121 mg); b.p. 90–100° (bath)/1.5 mm, identified (IR, ^{1}H-NMR). as *dehydrocycloisolongifolene* (**30**).[21]

Frac. 2. (petroleum ether/benzene 1:1, 50 ml×2; 252 mg): b.p. 145–155° (bath)/1.5 mm, characterised as acetate of **26**. IR: 1730, 1024 (actate); 850, 820 (C= CH). ^{1}H-NMR: 0.85 (*s*, 3H); 0.98 (*s*, 3H); 1.03 (*s*, 3H; 1.07 (*s*, 3H); 1.95 (*s*, 3H, CH_3COO); 4.80 (*d*×*d*, J_1 = 3 Hz, J_2 = 7 Hz $CHOCOCH_3$); 5.33 (*t*, J = 3 Hz, 1H, C=

CH). On saponification with 5% alcoholic KOH (reflux, 1 hr) and usual work-up, the required **26** was obtained, m.p. 88.5-90° (acetonitrile) (Lit.[23]: m.p. 95–96°). IR: 3240, 1045 (OH); 842 (C=CH), 817, 783. ^{1}H-NMR; 0.84 (s, 3H); 0.98 (*bs*, 6H); 1.15 (*s*, 3H); 3.80 (*d* × *d*, J_1 = 3 Hz, J_2 = 7 Hz, CHOH); 5.23 (*t*, J = 3 Hz, 1H, C=CH). MS: *m/e* 220 (M^+,35%), 176 (51), 160 (51), 132 (46), 119 (100), 118 (51), 105 (78), 91 (61), 77 (38), 41 (75). (Found: C, 81.68; H, 10.98. $C_{15}H_{24}O$ requires: C, 81.76; H, 10.98%).

5-*Hydroxy-isolongifolene*-1,2,4,4-d_4 (**33b**). Cycloisolongifolol-d_4 (**32b**) (870 mg), when exposed to AcOH HSO_4 exactly as above, and then processed in the same manner, furnished **33b** (320 mg), m.p. 87-88° (acetonitrile).

5-*Oxo-isolongifolene* (**27**. Alcohol **26** (550 mg) in acetone (20 ml) was treated at 0° with Jones' reagent till an orange colour persisted (1 ml). The mixture was kept at room temp (28°) for 3 hr and then worked up in the usual manner to furnish **27** (540 mg), b.p. 120–130° (bath)/1.5 mm.IR: 1740 (C=CH). ^{1}H-NMR: 0.77 (*s*,3H); 1.02 (*s*, 3H); 1.09 (*s*, 3H); 1.14 (*s*, 3H); 5.47 (*t*, J = 3 Hz, 1H, C=CH). MS: *m/e* 218 (M^+, 100%), 175 (78), 162 (22), 159 (15), 147 (44), 134 (23), 119 (28), 105 (23), 91 (24), 77 (14). (Found: C, 82.69; H, 10.59. $C_{15}H_{22}O$ requires: C, 82.51; H, 10.16%).

5-*Oxo-isolongifolene*- 1,2,4,4-d_4: (**34b**). Oxidation of **33b** (100 mg) with Jones' reagent, as above, furnished **34b** (70 mg).

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