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STUDIES IN SESQUITERPENES—XLIV

ISOLONGIFOLENE (PART 5): REARRANGEMENT OF ISOLONGIFOLENE EPOXIDE*

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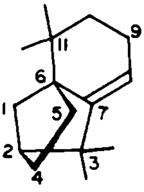
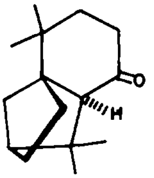
Abstract—Isolongifolene epoxide undergoes novel rearrangements on treatment with 1% HCl in $CHCl_3$ or on being exposed to active adsorbent (Al_2O_3, SiO_2-gel). The latter reaction leads to tetracarbocylic derivatives. These reactions fully substantiate the stereochemistry assigned earlier to isolongifolene epoxide.

EARLIER,[1] it has been described that the reaction of isolongifolene (I) with a $CHCl_3$ soln of perbenzoic acid (PBA) takes a distinctly different course, as compared to its normal reaction[2] with a benzene soln of PBA. The PBA-in-$CHCl_3$ reaction resulted in the formation of 8-oxoisolongifolane (II), besides an olefinic secondary alcohol. Working on the reasonable assumption that this difference in the reaction of PBA in the two different solvents, might have arisen from traces of hydrogen chloride being present in the $CHCl_3$ soln the reaction of isolongifolene epoxide (III) with 1% HCl in $CHCl_3$ has been investigated. This led to the formation of the same products, *viz.* ketone (II) and the olefinic secondary alcohol, in essentially the same yields, as obtained by the PBA-in-$CHCl_3$ reaction of isolongifolene. The secondary alcohol is now shown to possess the structure IV. Likewise, it was noticed that isolongifolene



I



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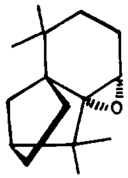

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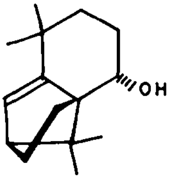
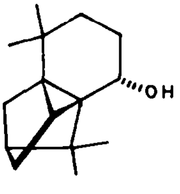


IV



V

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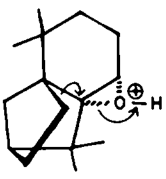
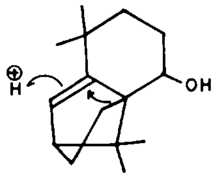
epoxide on exposure to active adsorbents (TLC) rapidly rearranged. It is now shown that treatment of isolongifolene epoxide with active Al_2O_3 (or SiO_2-gel) results in its isomerization to another secondary alcohol, formulated as V. These experiments form the subject matter of the present communication.

Rearrangement with 1% HCl *in* $CHCl_3$

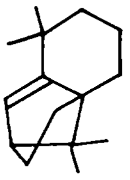
(±)-Isolongifolene epoxide on being exposed to 1% HCl in $CHCl_3$ at -10 to 0° smoothly passed into a ketone (~70%), readily identified as 8-oxoisolongifolane[2] (II) and an alcohol (15–20%; IR: OH 3400, 1045 and 1035 cm^{-1}), $C_{15}H_{24}O$, m.p. 144–145°. This alcohol is clearly olefinic (TNM, yellow color; IR: $-\underset{|}{C}{=}CH-$ 825 cm^{-1}; PMR, $CDCl_3$: $-\underset{|}{C}{=}C\underline{H}-\underset{|}{C}H-$, 1H doublet centred at 342·5 c/s, $J = 5$ c/s) and secondary (PMR, $CDCl_3$: 1H quartet centred at 233 c/s, with $J_1 = 10$ c/s and $J_2 = 7$ c/s) and can be formulated as IV, arising by way of a Wagner–Meerwein rearrangement (VI). In support of this structure, the alcohol on treatment with 2,4-dinitrophenylhydrazine in EtOH containing a little HClaq furnished, in good yield, the 2,4-DNP of ketone II. Evidently, a reverse 1,2-shift (VII) leading to the enol of II takes place in the first instance.



VI



VII



VIII

Pyridine-CrO_3 oxidation of the alcohol furnished the ketone with the expected spectral characteristics (IR: C=O 1705 cm^{-1}; C=C 1625, 822, 835 cm^{-1}; PMR: four quaternary methyls 51, 62·5, 68·5 and 70·5 c/s; one olefinic proton, 1H doublet centred at 341 c/s, $J = 3·5$ c/s). The ketone on Wolff–Kishner reduction, yielded the hydrocarbon VIII, which as expected* readily rearranged to isolongifolene under acid catalysis. This transformation further secures the structure IV.

It may be noted that for the transformation of isolongifolene epoxide to the alcohol IV, it is necessary that the oxirane ring must be α with respect to the ethylene bridge to permit the *trans*-antiparallel geometry[3] necessary for the rearrangement, thus confirming the earlier assignment[2] of stereochemistry III to isolongifolene oxide.

Rearrangement on active Al_2O_3, SiO_2-gel

Rearrangement of isolongifolene epoxide over Al_2O_3 was carried out by shaking it, in light petroleum soln with neutral adsorbent of Brockmann activity I.[4] The product, obtained in 75% yield, consisted of a hydrocarbon (48%), a ketone (9·5%) and an

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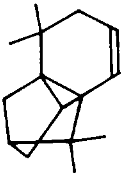
* This hydrocarbon is considered to be an intermediate in the genesis of isolongifolene from longifolene.[2]

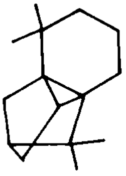
alcohol (42·5%). When SiO_2-gel was substituted for Al_2O_3, practically no hydrocarbon was formed and the product consisted of the same ketone (42%) and the same alcohol (50%), besides unchanged epoxide (8%). The ketone was readily identified as II.

The hydrocarbon, $C_{15}H_{22}$, is mono-olefinic, as on quantitative hydrogenation (PtO_2 catalyst) it yielded a dihydro derivative. Both the IR and PMR spectra clearly show that this olefinic linkage must be *cis*-disubstituted (IR: HC═CH 1640, 755 cm^{-1}; PMR: a complex 2H multiplet, ABX_2 type, located between 308 and 368 c/s). The fact that a mono-olefinic hydrocarbon has been produced from an epoxide, $C_{15}H_{24}O$, necessarily means that a new ring has been closed, which must be 3-membered in view of the behaviour of its dihydro derivative towards tetranitromethane[5] (TNM): practically no color with a 10% $CHCl_3$ soln of TNM, but a distinct yellow color with neat TNM. On these considerations, the hydrocarbon is formulated as IX and, this is supported by its UV absorption:[6] λ_{max} 215 mμ (ε, 5250). Final support for the structure IX was forthcoming from the fact that its dihydro derivative (X) readily passed into isolongifolene under acid catalysis.

In view of the above structure for the hydrocarbon, the alcohol (IR: OH 3250, 1015 and 990 cm^{-1}) accompanying it in the reaction mixture, was at once suspected to be V. This is clearly supported by its PMR spectrum: four quaternary Me's, 50·5, 58, 58 and 58 c/s; C<u>H</u>OH, 1H ill-resolved triplet centred at 255 c/s, $J = 4$ c/s. This conclusion was confirmed by its dehydration to the olefin IX, by heating it with Al_2O_3.[7,*]



IX



X

To check if the tetracyclic alcohol (V) is an intermediate in the HCl-catalyzed rearrangement of isolongifolene epoxide to the unsaturated alcohol (IV), V was exposed to 1% HCl in $CHCl_3$, under the reaction conditions used for the isomerization of the oxide to IV. However, under these conditions V, almost quantitatively, passed into the tetracyclic olefin IX.

In view of their structures, the hydrocarbons IX and X will, henceforth, be referred to as dehydrocycloisolongifolene and cycloisolongifolene respectively.

Cycloisolongifolene (X) and hydrocarbon (VIII) appear to be excellent substrates for probing the mechanism of formation of isolongifolene from longifolene and, such investigations are under way. Table 1 summarizes GLC and PMR data of these two hydrocarbons and those of isolongifolene.

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[*] Shaking a light petroleum soln of V with Al_2O_3, under the reaction conditions used for the isomerization of the oxide, failed to effect its dehydration to IX. On the other hand, increased reaction time for the Al_2O_3-induced oxide rearrangement, results in higher yields of the hydrocarbon (IX) at the expense of the corresponding V.

TABLE 1. GLC AND PMR CHARACTERISTICS OF ISOLONGIFOLENE, CYCLOISOLONGIFOLENE AND HYDROCARBON VIII

Compound	RRT[*]	PMR spectrum	
		Quaternary methyls (c/s)	olefinic proton (c/s)
Hydrocarbon VIII	0·609	43, 45, 60, 65	335·5, doublet $J = 3{\cdot}5$ c/s
Cycloisolongifolene (X)	0·714	48, 48, 56, 60	—
Isolongifolene (I)	1·0	50, 57, 57, 62	305, triplet, $J = 4$ c/s

[*] Retention time relative to that of isolongifolene; column: 5′ × 0·25″, 20% tung oil polymer on 60–80 mesh Chromosorb W; temp 185°; gas: H_2, 30 ml/min.

EXPERIMENTAL

For general remarks see Part XL of this series. PMR spectra were taken in 10–20% soln in CCl_4 (unless stated to the contrary) with TMS as the internal standard on a Varian A-60 spectrometer.

Isolongifolene epoxide used for the present work was the solid (±)-epoxide, m.p. 39–40°.

Rearrangement of isolongifolene epoxide with HCl–$CHCl_3$

Alcohol IV. A $CHCl_3$ soln of dry HCl (1%; 5 ml) was chilled to −10° to −12° and isolongifolene oxide (520 mg) was added in one lot and shaken till dissolved. The soln was left at the same temp for 1 hr and then at 0° for 24 hr. Water (100 ml) was then added and the $CHCl_3$ phase separated. The aqueous portion was extracted with ether (20 ml × 2) and the combined organic extracts washed with Na_2CO_3aq (10%; 20 ml × 3), brine and dried (Na_2SO_4). The solvent was flashed off and the residue showing two major spots on TLC (solvent system: toluene-EtOAc, 3:2), was chromatographed on neutral Al_2O_3 (grade II; 19 cm × 1 cm) with TLC monitoring.

Fraction 1:	light petroleum	5 ml × 4	25·8 mg of solid, m.p. 37–39°, unchanged oxide.
Fraction 2:	light petroleum	5 ml × 16	236·2 mg, liquid.
Fraction 3:	50% C_6H_6 in light petroleum	5 ml × 10	127·2 mg, liquid.
Fraction 4:	C_6H_6	5 ml × 3	
Fraction 5:	5% MeOH in C_6H_6	5 ml × 10	116 mg, solid, m.p. 106–113°

Fractions 2 and 3 showing identical TLC behaviour, were combined, distilled (b.p. 111–112°/1·5 mm) and identified (IR) as 8-oxo-7(α*H*)-isolongifolane[2] (II).

Fraction 5 on three crystallizations from hexane yielded white, feather-like crystals (90 mg), m.p. 138–140°. Repeated crystallizations from hexane raised the m.p. to 144–145°;[*] PMR spectrum ($CDCl_3$): quaternary Me's 51·5, 57, 63 and 66 c/s. (Found: C, 81·40; H, 11·10. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%).

Reaction of alcohol IV *with 2,4-dinitrophenylhydrazine.* A mixture of IV (200 mg), 2,4-dinitrophenylhydrazine (200 mg) in EtOH (10 ml) containing a few drops of conc HClaq was made clear by slight warming and left aside at room temp for 20 hr. The separated solid (250 mg) was collected and recrystallized from EtOH-pyridine to give silky orange needles, m.p. 244–245° (dec) identified as the 2,4-DNP of 8-oxoisolongifolane by mixed m.p. with an authentic sample.[2]

Pyridine-chromic acid oxidation of IV. Alcohol IV (440 mg, 0·002 mole) in pyridine (2 ml) was added to a suspension of CrO_3 (300 mg, 0·003 mole) in pyridine (2 ml). The reaction mixture was swirled from time to time and allowed to stand at room temp (25–28°) for 36 hr. After adding water (10 ml), the reaction mixture was filtered through a small layer of celite, which was washed with pentane. The filtrate was extracted with

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[*] This alcohol exists in another polymorphic form (identical IR and PMR spectra in soln), m.p. 125–126°; this form was often obtained by sublimation at 100°/1·5 mm.

pentane–ether (1:1; 10 ml × 4) and, the extracts washed with water, brine and dried (Na_2SO_4). Solvent was flashed off and the residue (428 mg) chromatographed over neutral Al_2O_3 (grade II; 16 cm × 1 cm).

Fraction 1:	light petroleum	10 ml × 2	—
Fraction 2:	50% C_6H_6 in light petroleum	10 ml × 3	355 mg, liquid.
Fraction 3:	C_6H_6	10 ml × 2	11·3 mg, liquid
Fraction 4:	1% MeOH in C_6H_6	10 ml × 3	50 mg, solid, m.p. 136–138°, unchanged alcohol.

Fractions 3 and 4 were combined and distilled to give the required ketone (341 mg), b.p. 125–130° (bath)/1 mm, n_D^{32} 1·4938. (Found: C, 82·52; H, 10·14. $C_{15}H_{22}O$ requires: C, 82·51; H, 10·16%).

Hydrocarbon VIII. The above ketone (100 mg) was added to an ethanolic soln of NaOEt (500 mg of Na dissolved in 15 ml of anhyd EtOH) containing hydrazine hydrate (85–90%, 2 ml) and, the reaction mixture heated in a sealed tube for 24 hr at 175 ± 5°. The product was isolated in the usual manner to yield VIII as an oil (47 mg), b.p. 100–105° (bath)/1·5 mm; TNM test, yellow color; IR spectrum: C═C 1625, 822 cm^{-1}. (Found: C, 88·31; H, 11·67. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

Isomerization of hydrocarbon VIII *to isolongifolene.* The above hydrocarbon (50 mg), dioxan (1 ml) and H_3PO_4 aq (d = 1·75, 0·25 ml) were mixed and heated on the steam-bath for 2 hr. The reaction mixture was worked up in the usual manner and the product (GLC pure) identified (GLC, IR) as isolongifolene.

Rearrangement of isolongifolene epoxide over Al_2O_3

Isolation of dehydrocycloisolongifolene (IX) *and alcohol* V. Isolongifolene oxide (1·07 g) in light petroleum (7 ml) was added to a slurry of Al_2O_3 (neutral/I, 50 g) in the same solvent (30 ml) and the mixture shaken (N_2) at room temp (25–28°) for 24 hr. This was transferred to a wide chromatographic column and the Al_2O_3 repeatedly washed first with light petroleum (20 ml × 8) and then with ether (20 ml × 4). The combined organic extracts were freed of solvent to give an oil (0·9 g), a part (0·78 g) of which was chromatographed over Al_2O_3 (neutral/I; 18·5 cm × 1·8 cm), under TLC monitoring (solvent: 5% EtOAc in C_6H_6):

Fraction 1:	light petroleum	10 ml × 7	338·6 mg, liquid
Fraction 2:	50% C_6H_6 in light petroleum	10 ml × 10	7·2 mg, liquid
Fraction 3:	C_6H_6	10 ml × 12	59 mg, liquid
Fraction 4:	1% MeOH in C_6H_6	10 ml × 8	14·5 mg, liquid
Fraction 5:	5% MeOH in C_6H_6	10 ml × 12	323 mg, solid, m.p. 90–96°

Fractions 1 and 2, showing identical TLC behaviour were combined and distilled to give IX as an oil (280 mg), b.p. 82°/2 mm (GLC pure), n_D^{30} 1·4912, d_4^{30} 0·9287, M_D 63·01 (calc. 62·91); PMR spectrum: quaternary Me's 51, 54, 58 and 64 c/s. (Found: C, 89·23; H, 10·99. $C_{15}H_{22}$ requires: C, 89·04; H, 10·96%).

Fractions 3 and 4 (same TLC behaviour) were combined, distilled and identified (IR) as 8-oxo-7(α*H*)-isolongifolane[2] (II).

Fraction 5 was recrystallized from hexane to give clusters of white, fine needles of V, m.p. 96–98°.* (Found: C, 81·89; H, 10·89. $C_{15}H_{24}O$ requires: C, 81·76; H, 10·98%).

Dehydration of alcohol V. Alcohol V (52 mg) was heated with Al_2O_3 (neutral/I, pretreated with 2% pyridine, [7b] 210 mg) at 225–230° for 2 hr. The product was worked up with light petroleum in the usual manner to give an oil (31 mg), which was chromatographed over Al_2O_3 (neutral/I) and the light petroleum eluates distilled (2 mm) to give a colourless liquid (14 mg), identified (GLC, IR) as IX.

Cycloisolongifolene (X). Hydrocarbon IX (300 mg) in ethanol (6 ml) was hydrogenated at 27°/710 mm over pre-reduced Adam's PtO_2 catalyst (50 mg), absorption of H_2 ceasing after 38 ml (one mole equiv) had been consumed. Usual work up gave after distillation a colourless liquid (230 mg, GLC pure), b.p. 65–66°/0·6 mm, n_D^{30} 1·4810, d_4^{30} 0·9124, M_D 63·65 (Calc. 63·38). (Found: C, 88·30; H, 11·81. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

Isomerization of cycloisolongifolene to isolongifolene

Cycloisolongifolene (107 mg), gl AcOH (0·5 ml), H_2SO_4 aq (50%, 0·15 ml) were mixed and left at room temp (25–28°) for 70 hr. Working up in the usual manner gave a product (90 mg), which was distilled (0·5 mm, bath 85–88°) to give an oil (73 mg) readily identified (GLC, IR) as isolongifolene.

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* Sometimes another modification (same IR in CCl_4 soln), m.p. 122–123° was obtained.

Isomerization of isolongifolene oxide over silica gel

Activated silica gel (chromatographic grade IIA,[8] 5·0 g) was added to isolongifolene oxide (119 mg) in pentane (1·5 ml) and shaken (N_2) for 2 hr at room temp (26°). The silica gel was transferred to a small chromatographic column and eluted as under:

Fraction 1:	light petroleum	15 ml	8·8 mg, unchanged oxide
Fraction 2:	50% C_6H_6 in light petroleum	15 ml	43·7 mg of ketone II (IR)
Fraction 3:	C_6H_6	15 ml	1·3 mg
Fraction 4:	10% MeOH in C_6H_6	15 ml × 2	55·6 mg, solid.

The last fraction was recrystallized from hexane to give white flakes, m.p. 96–98°, identified (mixed m.p., IR) as V.

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