Tetrahedron, 1960, Vol. 8, pp. 42 to 48. Pergamon Press Ltd. Printed in Northern Ireland

STUDIES IN SESQUITERPENES—XVII

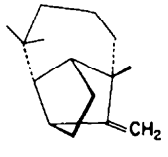
HYDRATION OF LONGIFOLENE*†

U. RAMDAS NAYAK and SUKH DEV
Organic Chemistry Department, Indian Institute of Science, Bangalore 12

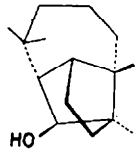
(*Received* 20 *May* 1959)

Abstract—Unlike the analogous case of camphene, hydration of longifolene with acetic acid–sulphuric acid in dioxane, yielded a strongly laevorotatory tricyclic isomer as the main product. At least three sesquiterpene alcohols resulted as side products, one of which could be correlated with longicamphor.

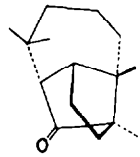
IN connexion with our attempts[1] to degrade longifolene (I) to a suitable azulene precursor, an easy route to longicamphor (III) was sought for. This ketone had been obtained previously by Naffa and Ourisson[2] by the oxidation of longiborneol (II), obtained from the corresponding longibornyl bromide via the Grignard derivative.



I



II



III

The preparation of longicamphor by this method appeared arduous, as the ketone could only be prepared in a poor (<15%) overall yield. Since camphene is known to yield isoborneol in an excellent yield on hydration with Bertram–Walbaum reagent,[3] this procedure appeared to be of great promise for the analogous preparation of longiborneol (II).‡ However, this reaction turned out to be a complex one and the chief product of the reaction was found to be an isomeric olefin, henceforth termed isolongifolene. This constituted ca. 60 per cent of the reaction product and the 'hydrated' material amounted to only ca. 30 per cent.§¶ The latter has been shown to consist of at least three acetates.

The acetate mixture resulting from the hydration of longifolene was saponified and the product fractionated to yield a liquid mixture of alcohols (ca. 89 per cent) and

* Presented at the Essential Oils & Aromatic Chemicals Symposium, Dehra Dun (India) October (1955).

† Abstracted from the Ph.D. thesis (Madras, 1957) of U. R. Nayak.

‡ Longifolene on hydrohalogenation gives only longibornyl halides [P. Ourisson and G. Ourisson, *Bull. Soc. Chim. Fr.* 1415 (1954)] in direct contrast with the case of camphene, which gives essentially only isobornyl derivatives. Likewise it may be anticipated that the hydration reaction would lead to longiborneol unlike camphene.

§ Naffa and Ourisson[2] also obtained similar results but did not examine the reaction products much further. These results were available to us after the publication of our preliminary note.[1]

¶ J. Tanaka and T. Aikawa [(*Rep. Osaka Ind. Res. Inst.* 30, 141 (1955)] have also recently investigated this reaction and could isolate only one alcohol (m.p. 108–109°) besides isolongifolene. We are thankful to these authors for sending us (Aug. 1957) the above report.

[1] U. R. Nayak and Sukh Dev, *Chem & Ind.* 989 (1954).

[2] P. Naffa and G. Ourisson, *Chem. & Ind.* 917 (1953); *Bull. Soc. Chim. Fr.* 1410 (1954).

[3] J. Bertram and H. Walbaum, *J. Prakt. Chem.* [ii] **49**, 8 (1894).

a crystalline secondary alcohol (A; ca. 10 per cent) (m.p. 107–108°). Though the m.p. of this alcohol is almost the same as that reported for longiborneol (II, m.p. 106–107°), the substance was shown to be different (*vide infra*). The liquid mixture could only be separated by an indirect method. The mixture, after oxidation with chromic acid, could be separated by semicarbazide into reactive (ca. 60 per cent) and non-reactive (30 per cent) portions. The latter fraction (infra-red absorption: 3484 and 1715 cm^{-1}) could be separated by chromatography into a new crystalline tertiary alcohol (B: ca. 20 per cent) (m.p. 92–94°) and a pure hindered ketone (ca. 80 per cent).

The hindered ketone

Longicamphor (III). The unreactive ketone ($\nu^{C=O}$ 1715 cm^{-1}; liquid), from its method of preparation, was considered to be the desired longicamphor, which is known[2] to be a hindered ketone. On reduction with sodium and n-propanol it gave the crystalline longiborneol (II), which was identified by comparison with an authentic sample of the alcohol prepared from longibornyl bromide by the method of Naffa and Ourisson.[2] Lithium aluminium hydride reduction of the ketone, on the other hand, gave a liquid mixture of the epimeric alcohols which could not be separated either by chromatography over alumina or via the 3,5-dinitrobenzoates.

Reactive ketone and the solid alcohol (A)

The compound regenerated from the semicarbazone (once recrystallized; m.p. 210–214°) showed a broad, partially resolved carbonyl band in the infra-red spectrum (liquid), two peaks at 1700 and 1735 cm^{-1} and a shoulder at 1715 cm^{-1} being prominent. This would indicate a mixture of at least three reactive ketones and from the relative intensities of the peaks, the 1700 cm^{-1} ketone appeared to be the major

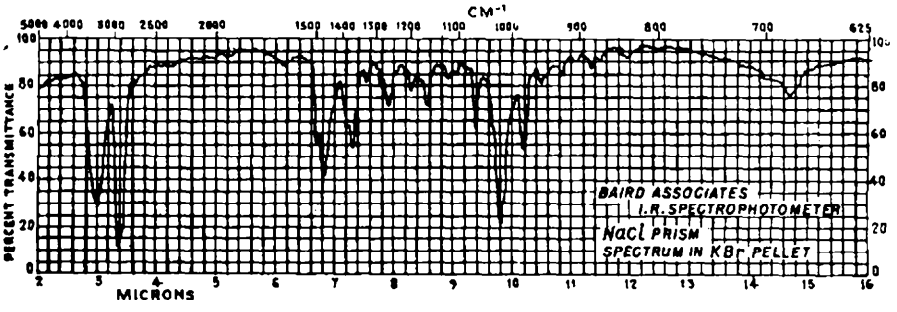


FIG. 1. Infra-red spectrum of solid alcohol (A).

component. When thoroughly purified semicarbazone (m.p. 215–216) was employed, the regenerated ketone was homogeneous and had a single peak in the carbonyl region at 1692 cm^{-1} (liquid). Reduction of this ketone with lithium aluminium hydride or with sodium-propanol gave a crystalline alcohol identified as the solid alcohol (A) by m.p. and mixed m.p. and also by preparing the 3,5-dinitrobenzoates which were identical. A further check was made by oxidizing the solid alcohol (A) when a single reactive ketone ($\nu^{C=O}$ 1692 cm^{-1}) was obtained. The infra-red spectrum of the alcohol is shown in Fig. 1.

The solid alcohol (B)

This compound was shown to be an alcohol from its absorption in the infra-red (Fig. 2) and since it resisted oxidation with chromic acid, it is presumably a tertiary alcohol. It was resistant to esterification and under the usual conditions failed to yield a 3,5-dinitrobenzoate.

*Isolongifolene**

By repeated fractionation of the isomerized hydrocarbon, isolongifolene could be isolated in a state of purity. The homogeneity of the product was checked by vapour-phase chromatography, when only a single non-resolvable peak was obtained. The hydrocarbon gives a yellow colour with tetranitromethane and it would appear from

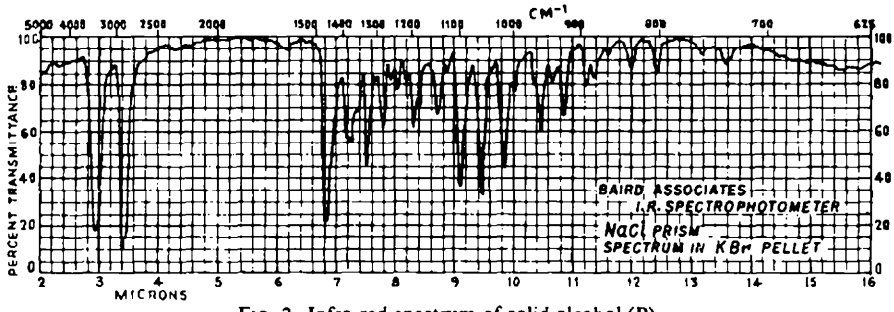


FIG. 2. Infra-red spectrum of solid alcohol (B).

its molecular refractivity (64·46) that isolongifolene is also tricyclic containing one ethylenic linkage. This was confirmed by quantitative hydrogenation over Adam's catalyst in acetic acid, when only one mole of hydrogen was absorbed to give a saturated hydrocarbon (negative tetranitromethane test). The infra-red spectrum of isolongifolane is quite different from that of longifolane, indicating a different carbon-skeleton for the hydrocarbon. In the C—H wagging region of the infra-red spectrum of isolongifolene a band at 820 cm^{-1} is the strongest and it would be reasonable to assign it to a trisubstituted olefinic linkage ($R_1R_2C = CHR_3$); it may be pointed out here that this band as well as a mild shoulder at 3050 cm^{-1} (=C–H stretching) are absent from the spectrum of isolongifolane. In the ultra-violet region, the new hydrocarbon showed only end absorption (ε_{210} 2180, ε_{215} 900, ε_{220} 265, ε_{225} 85) and this also is in accord with the occurrence of a trisubstituted ethylenic bond[4] in the molecule.

Preliminary work on these new products has shown that deep-seated rearrangements are involved and a systematic structure elucidation of isolongifolene has been taken up in this laboratory, in the first instance.

EXPERIMENTAL†

Isolation of (+)-longifolene

Pure longifolene was isolated from the 'Secondary Residue' obtained from the essential oil of *Pinus longifolia*, supplied by the Indian Turpentine & Rosin Co., Bareilly, U.P. (India).

* Recently J. Tanaka, [*Rep. Osaka Ind. Res. Inst.* No. 305 (1955); *Chem. Abstr.* **50**, 16708e (1956)] has reported the isomerization of longifolene with acetic acid–sulphuric acid to a new tricyclic hydrocarbon, which from its reported properties would appear to be identical with our isolongifolene.

† All melting and boiling points are uncorrected. The solvent extracts were dried over sodium sulphate. The infra-red spectra, unless otherwise stated, were determined by the Sadtler Research Laboratories, Philadelphia.

[4] P. Bladon, H. B. Henbest and G. W. Wood, *J. Chem. Soc.* 2737 (1952).

Secondary Residue (2754 g) was subjected to a preliminary fractionation through a helices-packed column (total condensation partial take-off type) and the main fraction (b.p. 116–120°/10 mm; $\alpha_D > +30°$; 2087 g) rich in longifolene was then systematically fractionated through another column* (30 theoretical plates). The rectification was carried out under reduced pressure (16 mm) employing a high reflux ratio (25 : 1). The charge was divided into 95 fractions and the course of fractionation was followed by observing the boiling point, refractive index and optical rotation for each fraction. By mixing the corresponding fractions of very similar properties three main cuts of the distillate were obtained: the earlier fraction (215 g), b.p. 117–126°/16 mm, having lower refractive index and rotation, the middle fraction (1241 g), b.p. 127–128°/16 mm, α_D +38° to +43·3° and the last fraction, (581 g), b.p. 129–139°/16 mm, $\alpha_D < +38°$. The second fraction (59%) which constituted pure longifolene was distilled over sodium and used for the present investigations. An analytical sample of longifolene had b.p. 118–119°/10 mm, n_D^{26} 1·5015, d_4^{26} 0·9319, M_D 64·71 (Calc. for $C_{15}H_{24}F_1$ 64·45), α_D +43·1° (homogeneous).

Hydration of (+)-longifolene

By following the usual Bertram–Walbaum reaction, the 'hydrated' material could only be obtained in a poor yield (ca. 15%) and it required a series of experiments to determine the nearly optimum conditions of hydration. In these experiments the variables studied were the source of the anion (acetic acid, formic acid, chloracetic acid), a strong proton source (sulphuric acid, perchloric acid), solvent (dioxane, methyl cellosolve), catalyst, time and temperature.

The following experimental conditions were found to be most satisfactory. Longifolene (200 g), glacial acetic acid (500 ml) and sulphuric acid (50% v/v; 40 ml) were mixed and dioxane (475 ml) was added to get a homogeneous solution. The reaction mixture was kept at room temp (22–24°) for 61 hr, warmed to 50 +· 2° for 10 hr and poured into water (600 ml). The organic layer was separated and the aqueous portion extracted with petroleum ether (50 ml × 3) after addition of ammonium sulphate. The oil was combined with the solvent extracts, washed with water till neutral, dried and the solvent removed through a column to obtain a deep brown liquid residue. The experiment was repeated with another lot (200 g) of longifolene and the crude hydration product obtained was combined with the earlier lot and fractionated to yield two products, isolongifolene and the acetate mixture. The former was obtained as a colourless mobile liquid, b.p. 119–122°/10 mm, n_D^{25} 1·4985, α_D −77°, yield 242 g (60·5%), and the latter distilled over as a colourless viscous liquid, b.p. 149–152°/9 mm, n_D^{25} 1·4925, d_4^{25} 1·001, M_D 76·52 (Calc. 75·76), α_D +26·9°, yield 154·6 g (29·9%) (Found: C, 77·53; H, 10·39. $C_{17}H_{28}O_2$ requires: 77·41; H, 10·61%).

Saponification of the mixed acetates

The above acetate mixture (154 g), potassium hydroxide (49 g) dissolved in water (30 ml) and ethanol (190 ml) were mixed and refluxed on the steambath (7½ hr). Most of the alcohol was then distilled off from the reaction mixture, the residue poured into water and the organic layer separated. The aqueous solution was extracted with pet. ether (50 ml × 3) and the combined organic portions were washed free of alkali with water, dried and the solvent removed through a column. The yellow residue (138 g) was carefully fractionated. After a small amount (4·45 g) of fore-run, the main fraction consisting of the liquid alcohol mixture distilled over as a colourless very viscous liquid, b.p. 147–149°/9 mm, n_D^{27} 1·5070 d_4^{27} 0·9946, M_D 66·41 (Calc. 66·4), α_D + 24° (c = 4·6%; ethanol), yield 114·8 g (88·6%) (Found: C, 81·2; H, 11·73. $C_{15}H_{26}O$ requires: C, 81·1; H, 11·71%). The second fraction (2·4 g) having b.p. 127°/2·5 mm solidified overnight to a colourless waxy solid, m.p. 81–86°. A third fraction (10·3 g) was obtained from the residue (which had crystallized overnight) by taking it up in ethanol and distilling it separately to give a white waxy solid, b.p. 142–145°/5 mm.

Isolation of the solid alcohol (A)

The second fraction (2·4 g) dissolved in the minimum amount of pet. ether (3 ml) was cooled to O° to yield a white crystalline solid (0·65 g; m.p. 100–105°); two more recrystallizations furnished shining white silky needles, m.p. 107–108° (constant). The third fraction (9·85 g) on similar treatment yielded colourless crystals (2·45 g) whose m.p. and mixed m.p. with the above alcohol remained the same. It had $[\alpha]_D$ +53·3° (c = 4·8%, ethanol) (Found: C, 80·35; H, 11·45. $C_{15}H_{26}O$ requires: C, 81·08; H, 11·71%).

* Supplied by the Emil Greiner Co., New York.

The 3,5-*dinitrobenzoate* was prepared from the solid alcohol (A) (220 mg), 3,5-dinitrobenzoyl chloride (230 mg), dry benzene (5 ml) and dry pyridine (0·1 ml) at room temp (60 hr). The crude product (300 mg; m.p. 134–139°) after two recrystallizations from benzene–petroleum ether mixture (1 : 1) gave colourless prismatic needles, m.p. 144–145° (Found: N, 6·50. $C_{22}H_{28}O_6N_2$ requires: N, 6·73%).

Oxidation to the ketone. The complex[5] prepared from chromium trioxide (1·5 g; 0·015 M) in dry pyridine (15 ml) was treated with a solution of the solid alcohol (A, 1·1 g; 0·005 M) in dry pyridine (11 ml) and kept at room temp (24–26°) for 42 hr. The reaction mixture was diluted with water (100 ml) and the product steam-distilled; the distillate (500 ml) was extracted with pet. ether (30 ml × 5), washed neutral with water, dried and the solvent removed. Distillation of the residue gave a colourless liquid, b.p. 120–125°/3 mm, yield 0·8 g (73%).

The *semicarbazone* prepared by the sodium acetate method and recrystallized from ethanol, was obtained as white crystals, m.p. 211–213°, mixed m.p. with the reactive ketone semicarbazone (*vide infra*) was undepressed.

Oxidation of the liquid alcohol mixture and separation of the ketones

A typical experiment was as follows: To a solution of the alcohol (10·2 g) in glacial acetic acid (40 ml) was added dropwise (35 min) a solution of chromic acid (7·5 g) in 80% acetic acid (100 ml), under stirring, at room temp. The exothermic reaction was controlled by external cooling so that the reaction temp did not exceed 40–50°. The stirring was continued for another 2 hr and the reaction mixture left at room temp (64 hr); diluted with water (500 ml), extracted with pet. ether (30 ml × 5), washed with bicarbonate solution and with water till neutral, dried and the solvent flashed off through a column. Distillation of the residue gave a colourless mobile liquid, b.p. 111–112°/1·5 mm, yield 8·65 g (85·6%).

Isolation of the reactive ketone as semicarbazone. The above oxidation product (8·65 g) was treated with a saturated solution of semicarbazide hydrochloride (6·0 g) and fused sodium acetate (5·6 g) in water (25 ml). Ethanol (50 ml) was added to obtain a clear solution and soon after, the white crystalline derivatives separated. After 4 days this was filtered, washed with water and dried; m.p. 195–200° (dec), yield 5·52 g (50·5%). Three recrystallizations of the crude derivative (2 g) from aqueous ethanol gave shining white crystals (0·3 g), m.p. 215–216° (dec) (Found: C, 69·29; H, 9·75; N, 15·12. $C_{16}H_{27}ON_3$ requires: C, 69·31; H, 9·75; N, 15·16%).

The 2,4-*dinitrophenylhydrazone* was prepared via the semicarbazone as follows. To a solution of 2,4-dinitrophenylhydrazine (200 mg), conc sulphuric acid (1 ml), water (3 ml) and ethanol (10 ml) was added the pure semicarbazone (300 mg). After keeping at room temp overnight, the orange precipitate was filtered (300 mg; m.p. 130–133°) and twice recrystallized from aqueous ethanol to obtain orange needles m.p. 156–158° (Found: N, 13·81. $C_{21}H_{28}O_4N_6$ requires: N, 14%).

Isolation of the unreactive portion from mother liquor. The first mother liquor was diluted with water till turbid, warmed on the water bath till the solution was clear and left aside at room temp for 10 days. After filtering off a small quantity (250 mg; m.p. 195–199°) of the precipitated solid, the filtrate was steam-distilled; the distillate (ca. 800 ml) was extracted with pet. ether (30 ml × 4), washed with brine till neutral, dried and the residue, after removal of solvent, was distilled to obtain a colourless mobile liquid, b.p. 110–112°/1·5 mm, n_D^{24} 1·4995, yield 2·5 g (29% of the ketone mixture). In another experiment the unreactive portion was worked up by ether extraction.

Reactive ketone

Regeneration from semicarbazone. The semicarbazone (18·55 g; m.p. 210–214°) and a saturated solution of oxalic acid (45 g in 120 ml of water) were mixed and directly steam-distilled. The distillate (1300 ml) was extracted with pet. ether (30 ml × 9) and worked up as usual to yield a colourless mobile liquid, b.p. 129°/4 mm, n_D^{27} 1·4980, d_4^{27} 0·9902, M_D 65·14 (Calc. 64·9), $[\alpha]_D$ +36·1° (c = 5%; ethanol), yield 13·45 g (91%) (Found: C, 81·61; H, 10·89. $C_{15}H_{24}O$ requires: C, 81·83; H, 10·91%).

Reduction to the solid alcohol (A)

(i) *With lithium aluminium hydride.* To a slurry of the hydride (100 mg) in dry ether (40 ml) was added, with stirring, a solution of the ketone (550 mg) in the same solvent (15 ml) at room temp (29°) and stirred for 2 hr. The excess of the hydride was decomposed by adding ice-water and the complex

[5] G. I. Poos, G. E. Arth, R. E. Beyler and L. H. Sarett, *J. Amer. Chem. Soc.* 75, 422 (1953).

hydrolysed with ice-cold dil sulphuric acid (10 ml). Usual work up gave the crude alcohol as a colourless solid (520 mg; m.p. 86–94°) which was thrice recrystallized from pet. ether to yield silky white needles, m.p. 105–106°, undepressed on admixture with the solid alcohol (A).

The 3,5-*dinitrobenzoate* of the crude alcohol (m.p. 86–94°), prepared in the usual way and recrystallized thrice from benzene–pet. ether at 0° deposited colourless crystals, m.p. 137–139°; mixed m.p. with the derivative of the solid alcohol (A) showed no depression.

(ii) *With sodium-n-propanol.* To a solution of the ketone (500 mg) in dry n-propanol (30 ml) kept on the steam-bath, pieces of sodium (1·5 g) were added in 4 lots during 40 min; after another 3 hr the excess of propanol was removed under suction; water (200 ml) was added, extracted with pet. ether (20 ml × 3), washed with water, dried and the solvent removed. The residue (520 mg) solidified slowly which had m.p. 80–84°; on admixture with the solid alcohol (A) the m.p. was raised to 91–97°.

Separation of the solid alcohol (B) from longicamphor

The unreactive portion (11·06 g) in dry pet. ether (20 ml) was chromatographed over alumina (Basic/I; 140 g; 34·5 × 2·4 cm). Elution with pet. ether (520 ml) gave a liquid (longicamphor; 8·52 g) and further washings with ether (280 ml) yielded the crystalline solid alcohol (B) (2·36 g), m.p. 82–90°. Repeated recrystallizations from n-hexane at 0° gave fine silky white clusters of needles, m.p. 92–94°, $[\alpha]_D$ −6·1° (*c* = 4·1%; ethanol) (Found: C, 81·47; H, 11·73. $C_{15}H_{26}O$ requires: C, 81·08; H, 11·71%). Mixed m.p. with the solid alcohol (A) was depressed to 62–75° and with authentic longiborneol was lowered to 62–74°.

Longicamphor

The above pet. ether eluterate was fractionated to give a colourless mobile liquid, b.p. 100°/0·6 mm, n_D^{26} 1·4990, d_4^{26} 0·9949, M_D 64·95 (calc. 64·9), $[\alpha]_D$ +18·8° (*c* = 5·3%; ethanol) (yield: 24% of the oxidation mixture; ca. 6% based on longifolene) (Found: C, 81·44; H, 10·90. $C_{15}H_{24}O$ requires: C, 81·83; H, 10·91%). Naffa and Ourisson[3] report b.p. 160–165°/15 mm, n_D^{20} 1·4989, $[\alpha]_D$ +22° (*c* = 5·8%; ethanol).

Reduction to longiborneol. To a solution of the ketone (500 mg) in dry n-propanol (30 ml) were added sodium pieces (1 g) and kept at room temp (20 min); another lot of sodium (500 mg) was then added and refluxed on the water bath (2 hr) and worked up as described previously to give a pale yellow solid (500 mg; m.p. 82–100°) which was chromatographed over alumina (6 g). The main fraction (m.p. 100–105°) eluted by pet. ether was sublimed on the steam-bath under vacuum (water-pump) to obtain glistening white crystals, m.p. 105–107° (Found: C, 81·11; H, 11·76. $C_{15}H_{26}O$ requires: C, 81·08; H, 11·71%). Mixed m.p. with an authentic sample of longiborneol showed no depression.

The 3,5-*dinitrobenzoate* prepared in the usual fashion and recrystallized from benzene–pet. ether furnished colourless needles, m.p. 155–156° (Found: N, 6·64. $C_{22}H_{28}O_6N_2$ requires: N, 6·73%).

Isolongifolene

Isolongifolene (235 g) having α_D −77° was subjected to precise fractionation in the "Emil Greiner's column and in all, 24 fractions were collected, the course of fractionation being followed by noting the b.p., n_D and M_D for each cut (ca. 10 ml). Fractions 5 to 22 having b.p., 112 to 114°, α_D −80·4 to −83·8° and $n_D^{25.5}$ 1·4980 to 1·4990 were mixed up (164·3 g) and distilled over sodium to yield isolongifolene as a colourless mobile liquid, b.p. 82–83°/0·4 mm, $n_D^{26.5}$ 1·4980, $d_4^{26.5}$ 0·9292, M_D 64·46 (calcd. for $C_{15}H_{24}F_1$ 64·43), α_D −82·2° (homogeneous), $[\alpha]_D$ −78·1° (*c* = 5·5%; ethanol) (Found: C, 88·08; H, 11·81. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

Isolongifolane. Hydrogenation of isolongifolene failed to take place over Adam's catalyst in alcoholic solution but in acetic acid it readily absorbed 1·05 mole of hydrogen at room temp and press to yield the saturated dihydro compound. Isolongifolane, thus obtained, was a colourless mobile liquid, b.p. 84°/0·4 mm, $n_D^{26.5}$ 1·4930, $d_4^{26.5}$ 0·9272, M_D 64·57 (Calc. 64·87), α_D +4° (homogeneous) (Found: C, 87·33; H, 12·56. $C_{15}H_{26}$ requires: C, 87·38; H, 12·62%). Infra-red absorption:* 1344, 1331, 1316(st), 1293(st), 1274, 1240(st), 1200, 1172, 1160, 1127(st), 1103, 1070, 1060, 1030, 958(st), 944, 925, 907, 887, 870(st), 840 and 777 cm^{-1}.

Longifolane. Longifolene (2·37 g) on catalytic reduction over Adam's catalyst (50 mg) readily absorbed 1·06 moles of hydrogen at room temp and press during 2½ hr. Longifolane, thus prepared,

had b.p. 118°/4 mm, n_D^{25} 1·4942; negative tetranitromethane test. Infra-red absorption:* 1307, 1284, 1228, 1216, 1203, 1187, 1160, 1140(st), 1122(st), 1090(st), 1055(st), 1018(st), 982(st), 957(st), 944, 878(st), 861, 840, 810 and 768 cm^{-1}.

Vapour phase chromatography of isolongifolene was carried out on a Perkin–Elmer Vapor Fractometer, model 154 B. A 2-meter "Siliconecelite" column, at 225° with a column pressure of 28 lb/in² and a flow rate of 5·0, was employed. Helium was used as the carrier gas and a 0·002 ml sample was injected. This analysis was done at the Noyes Laboratories, University of Illinois, Urbana and the authors wish to express their sincere thanks to Prof. E. J. Corey for these facilities.

* Determined on a Perkin–Elmer double-beam instrument.