

27. β -Phellandrene.

By A. KILLEN MACBETH, GILBERT E. SMITH, and TRUSTHAM F. WEST.

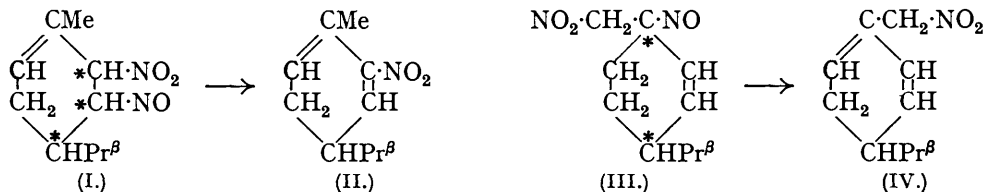
The α -nitrosites of *l*- β -phellandrene from Canada balsam oil and of *d*- β -phellandrene from water-fennel oil have been prepared and examined. Confusion might arise between *d* (or *l*)- β -phellandrene α -nitrosite and *l* (or *d*)- α -phellandrene β -nitrosite, as their melting points lie fairly close together and the specific rotations are of the same sign and of similar magnitude. The mutarotation of β -phellandrene α -nitrosite, however, proceeds slowly and the rotation does not fall to half the initial value. β -Phellandrene is further identified by the conversion of the nitrosite into nitro- β -phellandrene, which on reduction yields cuminal. Oxidation, according to conditions, leads to phellandral or 4-isopropyl- Δ^2 -cyclohexen-1-one. By these methods the presence of β -phellandrene in Canada balsam oil has been definitely established. Its absorption spectrum in hexane shows a maximum at 2312 μ . with $\log \epsilon$ 3.96.

THE critical examination of the oil of *Eucalyptus cneorifolia* gave evidence of the occurrence of both α - and β -phellandrene in the terpene fractions, and it was therefore desirable to secure authentic specimens of these hydrocarbons for comparison purposes. Water-fennel oil from the fruits of *Phellandrium aquaticum*, L. (Wallach, *Annalen*, 1904, 336, 1; Berry, Macbeth, and Swanson, J., 1937, 1448) was indicated as a source of *d*- β -phellandrene, and the oil of *Pinus contorta*, which has been reported to consist almost

entirely of *l*- β -phellandrene (*U.S. Dept. Agric. For. Serv. Bull.*, 1913, **119**, 26), was sought as a source of this hydrocarbon, but was unobtainable. A survey of the literature did not disclose any readily obtainable oil which would yield substantially pure *l*- β -phellandrene, but fortunately the recent examination of the oil of *Abies balsamea*, Miller (Smith and West, *J. Soc. Chem. Ind.*, 1937, **56**, 300r) disclosed a new source of the levorotatory hydrocarbon, and further examination of the carefully fractionated material fully supports the original suggestion that it is *l*- β -phellandrene.

The nitrosites of *l*- α -phellandrene have been comprehensively studied by Read and his co-workers, but the derivatives of β -phellandrene have not received the same detailed attention. Pure *l*- α -phellandrene α -nitrosite has a melting point of 121—122° and a specific rotation in chloroform of + 142.6° (Smith, Hurst, and Read, *J.*, 1923, **123**, 1657), whereas the β -nitrosite has m. p. 105—106° and $[\alpha]_D - 156.3^\circ$ in the same solvent (Smith, Carter, and Read, *J.*, 1924, **125**, 930). The latter values might conceivably be confused with those of a β -phellandrene derivative, for we have found that *d*- β -phellandrene α -nitrosite melts at 102—103° and in chloroform has $[\alpha]_D - 165.7^\circ$ (compare Wallach, *loc. cit.*, p. 44, who recorded m. p. 102°, $[\alpha]_D - 159.3^\circ$). On the other hand, *l*- β -phellandrene α -nitrosite is found to have m. p. 101—102° and $[\alpha]_D + 165.3^\circ$ in chloroform (compare Smith and West, *loc. cit.*, m. p. 101—102°, $[\alpha]_D + 157.9^\circ$) and similar values are to be expected in the case of pure *d*- α -phellandrene β -nitrosite. Moreover, since the melting point is not a criterion of optical purity, such physical constants by themselves cannot be regarded as establishing the identity of β -phellandrene; and reports of the occurrence of this hydrocarbon in natural sources which are based on such determinations must be accepted with reserve until further proof is submitted. Thus the occurrence of *l*- β -phellandrene in the oils derived from *Cinnamomum zeylanicum* (Shintre and Rao, *J. Indian Inst. Sci.*, 1932, **15 A**, 84), *Abies nobilis* (Lynn and Nakaya, *J. Amer. Pharm. Assoc.*, 1933, **22**, 305), and *Abies lasiocarpa* (Schwartz, *Amer. J. Pharm.* 1936, **108**, 197) cannot be regarded as established in the absence of further proof.

Since the α - and the β -nitrosite of *l*- α -phellandrene can be converted into identical derivatives, it is evident that the substances are stereoisomers, and Read and his co-workers (*loc. cit.*) have shown that they may be differentiated by observing the specific rotations of their freshly prepared solutions in various solvents. Thus the α -nitrosite gives the highest value in benzene, whereas the β -nitrosite has a maximum specific rotation in chloroform. The mutarotation of the isomers also presents differences. There is a rapid initial fall in the rotation of the α -nitrosite, the original high dextrorotation showing an optical inversion after the lapse of some 24 hours; and a marked levorotation is finally attained. An initial rapid mutarotation towards zero was also found in the case of the β -nitrosite in all solvents, but optical inversion was observed only in acetone solution: and the maximum change observed in acetone, benzene, and chloroform solutions was, after some 24 hours, followed by a slow decline. The mutarotation changes of α -phellandrene nitrosites (I) are to be associated with the presence in the molecule of three asymmetric carbon atoms, two of which would appear to be susceptible to modification as centres of optical activity through tautomeric change (compare Read, *loc. cit.*; Wallach, *loc. cit.*, p. 19). Similar mutarotation changes are, however, not to be expected in the case of β -phellandrene nitrosite (III), for the molecule contains only two asymmetric carbon atoms, and these do not show the same association as those in the previous case. In chloroform solution both *d*- and *l*- β -phellandrene



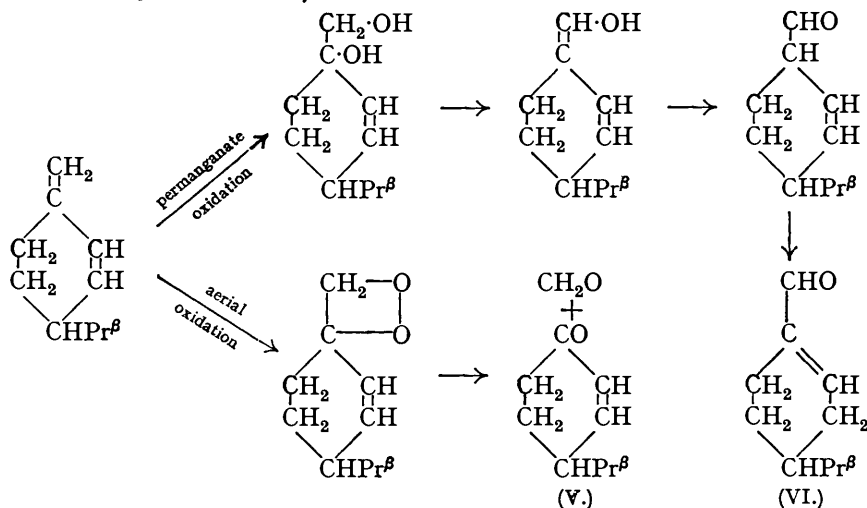
α -nitrosite show only a very slow mutarotation and no optical inversion takes place, since, in fact, the change in the specific rotation does not nearly attain zero. Although

Wallach reported the isolation of a β -phellandrene β -nitrosite (which, very remarkably, was inactive), we have not yet succeeded in preparing such a derivative.

For the further identification of β -phellandrene in Canada balsam oil we have converted the nitrosite into the nitrophellandrene by treatment with sodium ethoxide, and subjected the nitro-compound to reduction. Nitro- β -phellandrene (IV) differs from nitro- α -phellandrene (II) in that it cannot be rectified by distillation; and it also forms a solid compound on treatment with sodium hydroxide solution. The nitro- β -phellandrene derived from the *l*- β -phellandrene of Canada balsam oil was, after purification by steam distillation, laevorotatory, having $[\alpha]_D - 79^\circ$ in alcohol; that derived from *d*- β -phellandrene of water-fennel oil was dextrorotatory, $[\alpha]_D + 107.5^\circ$ in the same solvent.

Wallach (*Annalen*, 1895, 287, 376; *loc. cit.*) has shown that nitrophellandrenes on reduction give rise to carbonyl compounds together with basic products, and the identification of the carbonyl compound establishes the nature of the nitrophellandrene in question. Thus nitro- α -phellandrene gives rise to carvomenthone or carvotanacetone depending on the nature of the reducing agent, whereas nitro- β -phellandrene yields cuminal or dihydrocuminal according to experimental conditions. Structural identity of the phellandrene of Canada balsam oil and of water-fennel oil was thus established by the isolation of cuminal, the derivatives of the experimental aldehyde being identical with those derived from authentic material.

Further proof is found in the oxidation of the β -phellandrene from these sources. Phellandral (VI) was isolated *via* the glycol and identified as the product of permanganate oxidation, whereas aerial oxidation gave rise to 4-isopropyl- Δ^2 -cyclohexen-1-one (V) (Wallach, *Annalen*, 1905, 343, 28).



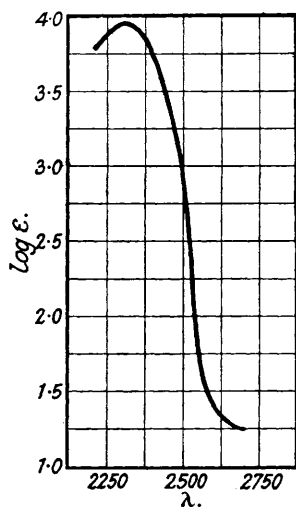
As the present sample of *l*- β -phellandrene from Canada balsam oil may be assumed to be very pure, its absorption spectrum was examined. The main fraction had b. p. $52^\circ/12$ mm., d_{15}^{15} 0.8497, n_D 1.4800, $\alpha_D - 44.1^\circ$ (homogeneous) and $[\alpha]_D^{20} - 51.9^\circ$. Its solution in hexane showed selective absorption of high intensity with a maximum at 2312 Å. and $\log \epsilon$ 3.96 due to the conjugated ethylene linkages. Allsopp (*Proc. Roy. Soc.*, 1934, A, 143, 624) has shown that 1:3-cyclohexadiene exhibits well-defined selective absorption with maxima at 1850 Å. ($\log \epsilon$ 4.75), 2560 Å. ($\log \epsilon$ 4.0), and 2680 Å. ($\log \epsilon$ 3.8). The first maximum is outside the region examined by us, and the other maxima due to the conjugation of the ethylene linkages within the ring are modified to the single maximum at 2312 Å. in β -phellandrene, where only one of the conjugated linkages is in the ring itself.

EXPERIMENTAL.

1- β -Phellandrene α -Nitrosite.—The freshly distilled essential oil from Canada balsam, dried over sodium sulphate, gave on careful fractionation a product, b. p. $78^\circ/24$ mm., which

consisted essentially of *l*- β -phellandrene and had b. p. 178—179°/758 mm., d_{15}^{25} 0.8497, n_D^{20} 1.4800, $\alpha_D - 43.2^\circ$, $[\alpha]_D^{20} - 50.6^\circ$ (Smith and West, *loc. cit.*). Redistilled, it gave a main fraction, b. p. 53°/12 mm., $\alpha_D^{20} - 44.1^\circ$, $[\alpha]_D^{20} - 51.9^\circ$. The absorption spectrum in hexane (figure) is characterised by a maximum at 2312 Å., $\log \epsilon$ 3.96.

l- β -Phellandrene (100 c.c.) was dissolved in light petroleum (600 c.c.), mixed with sodium nitrite solution (210 c.c.), and cooled below 0°, and glacial acetic acid (100 c.c.) at 0° stirred in. After standing for some time in the freezing mixture, the crude nitrosite was filtered off, washed successively with cold water and alcohol, and dissolved in chloroform; to the filtered solution, methyl alcohol was added to precipitate the nitrosite (16.3 g.). The product can be further purified by crystallisation from acetone or by repetition of the chloroform-methyl alcohol treatment. Refrigeration of solutions is desirable on account of the solubility of the nitrosite. Four crystallisations from acetone gave a product, m. p. 101—102°, with $[\alpha]_D^{20} + 160^\circ$, but in one case the specific rotation was as high as +167°. Repurified twice from chloroform and methyl alcohol, a sample had m. p. 100° and $[\alpha]_D^{20} + 169^\circ$ (*c*, 1.255 in chloroform). In another experiment, repeated treatment with chloroform and methyl alcohol gave a nitrosite, m. p. 101—102°, which had an initial specific rotation in chloroform (*c*, 1.255) of +165.3° at 25° and showed the following changes when kept in a thermostat at this temperature: after 16 hours, +130.7°; after 64 hours, +124.3°; after 92 hours, +117.1°; after 168 hours, +105°.



d- β -Phellandrene α -Nitrosite.—Water-fennel oil when distilled under reduced pressure yielded, amongst others, the following fractions which gave a strong phellandrene test: (a) b. p. 41—47°/7 mm.; $d_{15}^{15.5}$ 0.8575, $[\alpha]_D + 20.8^\circ$; (b) b. p. 44°/4 mm., $d_{15}^{15.5}$ 0.8564, $[\alpha]_D + 18.85^\circ$; and (c) b. p. 44—59°/4 mm., $d_{15}^{15.5}$ 0.8509, $[\alpha]_D + 16.16^\circ$ (Berry, Macbeth, and Swanson, *loc. cit.*). The α -nitrosite prepared from fractions (a) and (b) as in the preceding case, when purified by repeated treatment with chloroform and methyl alcohol, had m. p.'s ranging from 99° to 102—103° in different experiments and $[\alpha]_D$ values from -159° to -165.7° . The nitrosite showed the slow mutarotation characteristic of β -phellandrene α -nitrosite, optical inversion not being experienced. At laboratory temperature the following changes were recorded from an initial $[\alpha]_D$ in chloroform solution of -162.6° ; after 7 days, -127.5° ; after 9 days, -111.2° ; after 12 days, -97.2° .

d- and *l*-Nitro- β -phellandrene.—The nitrosite of β -phellandrene is converted into nitro- β -phellandrene by the action of sodium ethoxide at 30—40° and subsequent heating in a water-bath. The product, poured into cold water and extracted with ether after acidification with dilute sulphuric acid, gave, on removal of solvent, nitro- β -phellandrene as a yellow oil. It gave a reddish-yellow solid, insoluble in alcohol, when treated with half its volume of sodium hydroxide solution (50%). The nitro- β -phellandrene derived from *d*- β -phellandrene α -nitrosite, after steam-distillation, was dextrorotatory, $[\alpha]_D + 107.5^\circ$ (alcohol; *c*, 25), whereas that from the nitrosite of *l*- β -phellandrene was laevorotatory, $[\alpha]_D - 78.8^\circ$ under the same conditions. As the rectification did not involve large amounts of the nitrophellandrene, the rotations may be subject to modification in future work.

Reduction of Nitro- β -phellandrene.—It is unnecessary to isolate the nitro- β -phellandrene for reduction, and the solution after treatment of the nitrosite with sodium ethoxide is diluted with a further volume of alcohol, and metallic sodium added under reflux. To a solution of sodium (7.2 g.) in absolute alcohol (150 c.c.), *l*- β -phellandrene α -nitrosite (15 g.) was slowly added, and the thick mass heated in the water-bath for 15 minutes. After the addition of a further volume of absolute alcohol (450 c.c.), sodium (35 g.) was gradually added under reflux. After removal of the greater part of the alcohol with steam the residue in the flask was acidified with dilute sulphuric acid and subjected to steam-distillation; an inactive oil (2.6 c.c.) recovered from the distillate by extraction with ether gave a semicarbazone, m. p. 212° after recrystallisation from methyl alcohol, and a 2:4-dinitrophenylhydrazone, m. p. 244—245° after crystallisation from alcohol-chloroform. These showed no depression of m. p. when mixed with the corresponding authentic derivatives of cuminal.

d- β -Phellandrene α -nitrosite similarly gave cuminal on reduction with sodium (compare Wallach, *Annalen*, 1905, 340, 6).

Oxidation Experiments.—(a) A fraction of water-fennel oil (80 c.c.) rich in *d*- β -phellandrene was placed in a quartz flask with water (50 c.c.) and agitated by gentle bubbling of oxygen during irradiation (6 hours) with light from the mercury lamp. Estimation of aldehydes (hydroxylamine method) gave an aldehyde content of approximately 16%, calculated as $C_9H_{14}O$. As the decomposition of the peroxide theoretically gives rise to a molecule of formaldehyde together with a molecule of 4-isopropyl- Δ^2 -cyclohexen-1-one, this is equivalent to some 3% of the latter. On shaking with 35% neutral sodium sulphite solution (100 c.c.) the liberated sodium hydroxide required 7.3 c.c. of 3N-sulphuric acid for neutralisation. This is equivalent to reaction of 3.02 g. of ketone, a value in good agreement with the deduced percentage. On treatment of the sulphite solution in the usual way 1.1 c.c. of purified ketone were recovered. This had $\alpha_D + 46.7^\circ$ and gave a *p*-nitrophenylhydrazone, m. p. 167° , which was not depressed when mixed with an authentic derivative of *d*-4-isopropyl- Δ^2 -cyclohexen-1-one.

(b) A sample of oil rich in *l*- β -phellandrene (60 c.c.), mixed with water (50 c.c.), was shaken in a 2.5 l. bottle with oxygen and left in sunlight for 2 weeks, oxygen being introduced every few days and the mixture shaken from time to time. Steam-distillation gave 20 c.c. of oil, and a polymerised product remained. The usual sodium sulphite treatment gave 1.5 c.c. of purified levorotatory ketone, which formed a *p*-nitrophenylhydrazone, m. p. 168° (Found: C, 66.0; H, 6.6. Calc.: C, 65.9; H, 6.7%), and a 2:4-dinitrophenylhydrazone, m. p. 137 — 138° . The m. p.'s were not depressed by the respective derivatives of *l*-4-isopropyl- Δ^2 -cyclohexen-1-one. Similar results were obtained on oxidation by irradiation as in the case of *d*- β -phellandrene.

(c) The alternative oxidation using 1% permanganate solution was carried out by modification of Wallach's method (*Annalen*, 1905, **340**, 1). 50 C.c. of fraction (b) of water-fennel oil (above) were shaken with 1 l. of 1% permanganate solution at 0° . When all the permanganate was decolorised, a further quantity of powdered permanganate was added in small amounts until oxidation was complete, the temperature being maintained at about 0° by the addition of ice. After removal of the manganese sludge, which was well washed, the combined filtrates were concentrated under reduced pressure, and the syrup extracted with chloroform. The glycol remaining on removal of the chloroform was distilled with 10% sulphuric acid (200 c.c.) and 0.5 c.c. of oil was recovered by ether extraction of the distillate. This was identified as phellandral by the 2:4-dinitrophenylhydrazone, m. p. 203 — 204° after crystallisation from alcohol-chloroform. The m. p. was not depressed by the corresponding derivative of *d*-phellandral.

l- β -Phellandrene on similar treatment also gave a pale yellow oil, which was identified as phellandral by formation of a semicarbazone, m. p. 203 — 204° .

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JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE.

THE RESEARCH LABORATORY, STAFFORD ALLEN & SONS, LTD., LONDON, E.C. 2.

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