106. *Phellandrene Nitrosites. Part I. The α- and the β-Nitrosite of l-α-Phellandrene.*

By P. A. Berry, A. Killen Macbeth, and T. B. Swanson.

Examination of the nitrosites of *l*-α-phellandrene shows that the α-nitrosite prepared by previous workers was isolated in a pure state, whereas the β-nitrosite was a contaminated product. It is now found that on crystallisation from acetone, methyl alcohol, and other solvents the β-nitrosite is readily converted in part into the α-isomer, but the yields are never large, as other mutarotation products are formed during the process. An explanation is thus provided of the discrepancies observed by previous workers in the specific rotations recorded for *l*-α-phellandrene β-nitrosite, which range from — 36° to — 160°. Specimens having a value as high as — 260° have now been obtained, but in view of the transmutation recorded it is possible that the final maximum value has not yet been attained.

The transmutation also throws light on the observed similarity of the crystalline products obtained on recrystallisation of the α- and the β-nitrosite from hot methyl alcohol (Smith, Carter, and Read, J., 1924, **125**, 930), since the products are in fact identical, consisting of the α-nitrosite in each case.

In a previous paper (J., 1937, 1443) it was shown that examination of the seasonal variation in the oil from the tips of *E. cneorifolia* disclosed the presence of remarkably high percentages of terpene hydrocarbons during the period of active growth. Nitrosite tests indicated that considerable quantities of phellandrenes were present in the hydrocarbon fraction, and oxidation experiments showed that β-phellandrene appeared to be one of the main constituents. Other unpublished work, however, indicated that α-phellandrene also was present, and it was therefore considered advisable before proceeding further with this problem to make a full examination of the phellandrene nitrosites with a view to studying the best methods of separation of the isomers in the pure state. The results obtained in the case of *l*-α-phellandrene are now submitted.

Schreiner (*Arch. Pharm.*, 1901, **239**, 90) prepared from eucalyptus oil phellandrene (species unrecorded) a crude nitrosite, which on fractional crystallisation was separated into two components. The dextrorotatory component, known as *l*-α-nitrosite, had a specific rotation of + 123·5° and melted at 120—121°, whereas the lævorotatory product, known as *l*-α-phellandrene β-nitrosite, melted at 105—106° and had a specific rotation of — 36°. Wallach (*Annalen*, 1904, **336**, 9) isolated substantially the same products. His specimens of the β-nitrosite melted at 105° and in chloroform solution had values of $[\alpha]_D$ — 40·817° and — 40·287°. The specific rotations of his preparations of the α-nitrosite were somewhat higher than Schreiner's (+ 135·93° and + 142·6°), but the melting point was lower (113—114°).

Smith, Hurst, and Read (J., 1923, **123**, 1657), repeating the preparation of *l*-α-phellandrene α-nitrosite from the hydrocarbon fraction of the oils of *E. dives* and *E. phellandra*, had no difficulty in isolating material melting at 121—122° and having the highest specific rotation recorded by Wallach (+ 142·6°); and later Smith, Carter, and Read (*loc. cit.*) isolated the α-nitrosite with substantially the same constants from the oil of *Melaleuca acuminata*. Detailed data on the mutarotation of the α-nitrosite under a variety of conditions were submitted by Read and his co-workers. We also have examined the α-nitrosite from the *l*-α-phellandrene of *E. dives* and fully concur with the results of these workers. Although the highest yields of nitrosite are obtained from samples of *l*-α-phellandrene of greatest specific rotation, the reaction is not affected to any extent by the presence of cineole, cymene or other inactive diluents, and the same nitrosites are always obtained. Birch (*Proc. Roy. Soc. N.S.W.*, 1937, **71**, 261) considers that the low optical values of specimens of *l*-α-phellandrene of low specific rotations from eucalyptus oils are due to the presence of cymene as a diluent. Accordingly we did not subject our preparations of *l*-α-phellandrene from *E. dives* to the rigorous treatment of Smith, Hurst, and Read, and the specific rotation of our material was frequently lower than theirs (— 112°).

Smith, Carter, and Read (*loc. cit.*), taking advantage of the different solubilities in carbon disulphide of the two nitrosites of *l*-α-phellandrene, succeeded in isolating the β-nitrosite in what has hitherto been regarded as a state of purity. Their product melted at 105—106° and had a specific rotation in chloroform of — 160° when freshly dissolved.

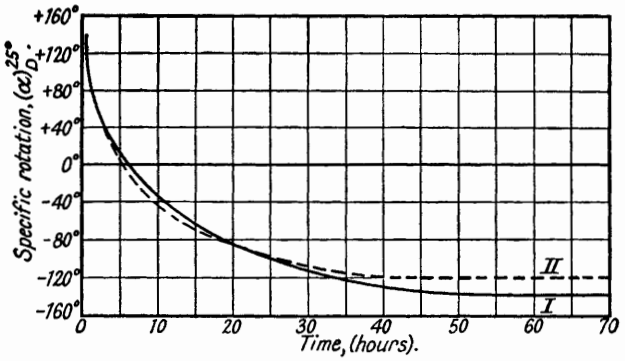
The conversion of both the α- and the β-nitrosite into chemically and optically identical preparations of nitrophellandrene shows conclusively that both are derived from *l*-α-phellandrene. The fact that their specific rotations were in the opposite sense and appeared to be of approximately the same magnitude suggested that the isomers might be optical antipodes; but such a view, already excluded by their different physical properties and their behaviour on mutarotation, is further disproved by the isolation of the β-nitrosite with a specific rotation as high as — 260° in the present work.

The accepted structure of α-phellandrene nitrosite contains three asymmetric carbon atoms and as those at the 2- and 3-positions would appear to be peculiarly susceptible to modification through tautomeric change, transmutation of the labile nitrosite to the stable form might thus be achieved.

No evidence has hitherto been available to show that the nitrosites are interconvertible, but the easy conversion of the labile β-nitrosite into the stable crystalline α-form has now been demonstrated. On crystallisation of samples of β-nitrosite melting at 96° and having $[\alpha]_D$ — 203° from hot acetone, the crystalline material recovered melted at 114° and had $[\alpha]_D$ + 141·6°. Analysis showed that no change in percentage composition had occurred; and the identity of the material with α-nitrosite was proved by its mutarotation curves, which were practically coincident with the standard curves for this compound (Figs. 1 and 2). The view that the process is actually a transmutation of the β-nitrosite and not merely a separation of traces of the less soluble α-nitrosite is supported by the fact that material precipitated from the mother-liquors is also dextrorotatory (+ 79°): and bearing in mind the observed mutarotation effects in this solvent at 25°, it would seem that the precipitation product must be considered as derived from α-nitrosite which has undergone partial mutarotation. Similar transmutation was observed with other solvents; a sample of β-nitrosite (m. p. 102°; $[\alpha]_D$ — 190°) on recrystallisation from hot methyl alcohol, for example, suffered inversion of rotation to + 132·9° and had the m. p. raised to 112—113°.

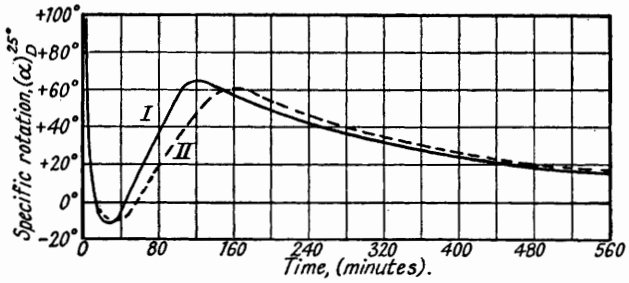
This transmutation throws light on discrepancies in the literature regarding the crystalline form of the α- and the β-nitrosite. Schreiner (*loc. cit.*) stated that the two compounds had different crystalline forms, but Smith, Carter, and Read (*loc. cit.*, p. 936) disputed this statement and showed that after recrystallisation from hot methyl alcohol both *l*-α-phellandrene α-nitrosite and *l*-α-phellandrene β-nitrosite gave long, fine needles resembling Schreiner's description of the α-form. The crystals were indistinguishable even with the aid of the polarising microscope and were in apparent agreement in all ordinary physical crystallographic respects. The optical rotatory powers do not appear to have been examined, but the results referred to above suggest that the substances were in fact identical, consisting of *l*-α-phellandrene α-nitrosite.

FIG. 1.



I. l-α-*Phellandrene α-nitrosite in chloroform.*
II. " *Converted* " *nitrosite in chloroform.*

FIG. 2.



I. l-α-*Phellandrene α-nitrosite in chloroform* + N/10-*piperidine.*
II. " *Converted* " *nitrosite in chloroform* + N/10-*piperidine.*

The transmutation also accounts for the different specific rotations recorded for the β-nitrosite, and clearly indicates that its extraction from the crude nitrosite must be carried out without delay, as nearly as possible with solvents at the ordinary temperature. Using such precautions, we had no difficulty in obtaining material with specific rotation of — 200° in freshly prepared chloroform solution, and on occasion isolated material with a rotation as high as — 260°. We are of opinion that material of still higher rotation may yet be available by further modification of the method of extraction.

Previous workers have pointed out that the melting point affords no satisfactory criterion of optical purity of the β-nitrosite, and Wallach (*loc. cit.*, p. 16) further directed attention to the fact that mixed melting points of the α- and the β-nitrosite did not show the depression usually observed on the admixture of compounds of different constitution. We have observed that the higher the rotation of our specimens of β-nitrosite the lower the melting point, and on admixture with pure α-nitrosite an intermediate value of melting

point is obtained. Thus samples of β-nitrosite melting at 102° and 94—95° were found on admixture with approximately equal amounts of α-nitrosite to melt at 105—106° and 103—105° respectively.

Experimental.

l-α-*Phellandrene*.—Piperitone was removed from a sample of *E. dives* oil ($d_{15°}^{15°}$ 0·9018; $[\alpha]_D^{20°}$ − 54·7°; piperitone 45% by vol.) by extraction with hot sodium sulphite solution (Read and Smith, *J. Soc. Chem. Ind.*, 1923, **42**, 339T). The residual oil after successive washing with sodium carbonate solution and water and drying over anhydrous magnesium sulphate had α_D − 48·7°. When distilled through a fractionating column packed with aluminium Lessing rings, the oil (2 l.) gave crude terpene (1·24 l.), b. p. 46—56°/6 mm. This was again fractionated, and 1 l. collected having b. p. 41—44°/4 mm. and α_D − 67·5°. This was extracted (8 times) with half-volume lots of 50% resorcinol solution to remove cineole (139 c.c. of crude cineole, α_D − 14°, were recovered on steam distillation of the extracts). The residual terpene after thorough washing and drying, when fractionated (twice), gave a product (500 c.c.) having the following constants, which, apart from the somewhat lower rotation, are in substantial agreement with the values recorded by Smith, Hurst, and Read: $d_{20°}^{20°}$ 0·8449; $d_{4°}^{20°}$ (vac.) 0·8436; α_D − 81·16°; $[\alpha]_D^{20°}$ − 96·21°, $n_D^{20°}$ 1·4757, whence $[R]_D = 45·47$.

At first only this pure material was used in the preparation of nitrosites, but in later work once-fractionated oil having α_D − 67° was used.

Preparation of α- and β-Nitrosites.—Smith, Hurst, and Read's method was used for the preparation of the crude nitrosites, 100 c.c. of the terpene fraction being used in each reaction. In the first experiments the separation scheme of Smith, Carter, and Read was employed, but this was modified somewhat in the later separations. The crude nitrosite (30 g.) from 100 c.c. of terpene, after being washed with alcohol and water, and dried between sheets of absorbent paper, was extracted (twice) with carbon disulphide (100 c.c.), the mixture being stirred to a thin cream, boiled, and filtered. Evaporation of the filtrate in a current of air left a residue, which was washed with methyl alcohol, crude β-nitrosite (1 g.), $[\alpha]_D^{20°}$ − 143·7°, being obtained. The residue (29 g.) left after the carbon disulphide extraction was dried on porous tile. It was still lævorotatory ($[\alpha]_D^{20°}$ − 16°) and was quickly dissolved by stirring into boiling chloroform (72 c.c.). After addition of methyl alcohol (250 c.c.) with rapid stirring, the mixture was placed in the refrigerator overnight and the solid was filtered off and washed with methyl alcohol (65 c.c.). The dried residue had $[\alpha]_D^{20°}$ + 26·6° and was worked up for pure α-nitrosite in the usual way. The filtrate and washings were brought to incipient precipitation by the addition of water (85 c.c.) with vigorous stirring, and the solution placed in the refrigerator for 24 hours. After filtration and washing with methyl alcohol (20 c.c.) a white amorphous solid (1·2 g.) was obtained having m. p. 96° and $[\alpha]_D^{20°}$ − 260·1° in chloroform (*c*, 1·25) (Found: N, 13·2%). The mutarotation curves of this sample of β-nitrosite in benzene and in acetone closely resembled the standard types. No difficulty was experienced in obtaining by this treatment 1—1·5 g. of β-nitrosite having rotations upwards of − 200°. The high rotation of the β-nitrosite is of course obtained at the expense of the yield, as the mild extraction leaves much material behind which is sacrificed in the subsequent purification of the α-nitrosite.

Transmutation of l-α-*Phellandrene* β-*Nitrosite into* l-α-*Phellandrene* α-*Nitrosite*.—Attempts to purify the samples of β-nitrosite by crystallisation invariably led to a considerable decrease in the optical value and suggested that some profound change was occurring. This was confirmed by the transmutation effects described below. On attempting to purify a sample of β-nitrosite ($[\alpha]_D$ − 144°) in the earlier part of the work it was observed that the crystals obtained melted at 108—109° and had a specific rotation of + 139·3°. On fractional precipitation of the mother-liquor, only dextrorotatory products were obtained. Other samples of the β-nitrosite gave similar results. For example, a specimen (1·4 g.), m. p. 95—96°, $[\alpha]_D^{20°}$ − 203°, when boiled for 5 minutes with 10 c.c. of acetone gave on crystallisation a product (0·3 g.), m. p. 113—114°, $[\alpha]_D^{20°}$ + 141·6° in chloroform (*c*, 1·264). The filtrate on evaporation to dryness in a rapid current of air gave a somewhat sticky residue (1·0 g.), which, on being washed with a little methyl alcohol, gave a pure white product, m. p. 100°, $[\alpha]_D^{20°}$ + 79·7° in chloroform (*c*, 1·258). A similar conversion carried out with material having $[\alpha]_D$ − 214° gave a crystalline product, m. p. 114—115° (Found: N, 13·2. Calc. for $C_{10}H_{16}O_3N_2$: N, 13·2%). The following values for the specific rotation in various solvents were observed at 20°: acetone (*c*, 1·247) + 175·6°; benzene (*c*, 1·171) + 240·8°; chloroform (*c*, 1·264) + 141·6° (compare the values for pure α-nitrosite given by Smith, Carter, and Read, *loc. cit.*; namely, acetone + 165·9°; benzene + 234·4°; chloroform + 142·6°). The mutarotation curves for the converted material in

chloroform and in chloroform containing N/10-piperidine are in excellent agreement with curves for pure α-nitrosite

Conversions were also observed on crystallisation from hot methyl alcohol. In a typical case a sample of β-nitrosite, m. p. 102°, $[\alpha]_D$ − 190° (chloroform), on recrystallisation yielded a mat of fine needles characteristic of the α-nitrosite. These had m. p. 112—113°, and $[\alpha]_D^{20°}$ + 132·9° in chloroform (*c* 1·243).

It would appear that the β-nitrosite has a lower m. p. as its lævorotation increases, the following values having been recorded during the work : $[\alpha]_D^{20°}$ − 260·1°, m. p. 95—96°; $[\alpha]_D^{20°}$ − 214°, m. p. 98—99°; $[\alpha]_D^{20°}$ − 200°, m. p. 99—100°; $[\alpha]_D^{20°}$ − 190°, m. p. 101—102°. Mixture of the α- and the β-nitrosite does not produce a depression in the m. p., but leads to an intermediate value, as has been mentioned above.

Mutarotation Curves.—The mutarotation effects of the nitrosites were in all cases examined at 25°. The concentrations were substantially the same in all cases, the solutions being of a strength similar to that used by Read and his co-workers in order to facilitate comparison. The curves were in all cases in close agreement with those previously published by these workers. The identity of " converted " nitrosite with *l*-α-phellandrene α-nitrosite is seen in Figs. 1 and 2.

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JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE. [*Received, November 8th,* 1938.]