259. *Observations on the Absorption Spectra of Terpenoid Compounds. Part VI.* " iso*Cadinene.*"

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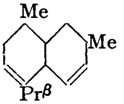
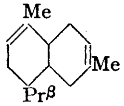
The so-called " *iso*cadinene " obtained by the action of hydrogen chloride on cade oil has been shown to be heterogeneous. By means of chromatography with spectroscopic control it has been demonstrated that one component absorbing light maximally at 2450 A. can be separated and is probably a hexahydrocadalene containing a conjugated diene system having the two ethylene linkages distributed between two rings. The other main component absorbs at wave-lengths < 2200 A. and may be a related ethylenic compound.

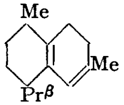
THE work of Campbell and Soffer (*J. Amer. Chem. Soc.*, 1942, **64**, 417) which necessitated the change of the structure (I) previously postulated for cadinene to (II) raises the question of the structure of the isomeric hydrocarbon *iso*cadinene.



(I.)



(II.)



(III.)

It was observed by Henderson and A. Robertson (*J.*, 1924, **125**, 1992) that attempts to hydrate cadinene by Bertram and Walbaum's method yielded not an alcohol but an isomeric unsaturated hydrocarbon which they termed *iso*cadinene and which from its physical constants appeared to be identical with the sesquiterpene first separated from oil of cade by Tröger and Feldman (*Arch. Pharm.*, 1898, **236**, 692; cf. Lepeschkin, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 126).

Henderson and J. M. Robertson (*J.*, 1926, 2811) considered that these two sesquiterpenes were identical, and suggested that *iso*cadinene was represented by (III), the formula proposed by Ruzicka and Capato (*Helv. Chim. Acta*, 1925, **8**, 259) for the hexahydrocadalene synthesised by them from nerolidol and bisabolene by the action of acid reagents. Unlike cadinene, *iso*cadinene did not give crystalline derivatives with halogen acids, and Henderson and J. M. Robertson based their conclusions on the close similarity of the physical constants as well as the production of cadalene by heating *iso*cadinene with sulphur. Cadalene is a 3 : 8-dimethyl-5-*iso*propylnaphthalene, and was synthesised by Ruzicka in 1922. The physical constants of the three products were as follows :

	B. p./11—12 mm.	*d.*	n_D.
*iso*Cadinene	124—126°	0·914	1·515
Cade oil sesquiterpene	124—128	0·918	1·515
Hexahydrocadalene (synthetic)	125—126	0·916	1·509

At the same time Henderson and J. M. Robertson stated that " the large exaltation appears to be characteristic of this compound (sesquiterpene from cade oil) and of *iso*cadinene, and may indicate a system of conjugated bonds, or, less probably, the admixture of monocyclic component ". They drew attention to the fact that Semmler and Jakubowicz (*Ber.*, 1914, **47**, 2252) by heating cadinene in an autoclave obtained a substance, b. p. 120—130/12 mm., *d* 0·9025, n_D 1·5083, which was considered to be a monocyclic sesquiterpene mixed with cadinene (cf. J. M. Robertson, Kerr, and Henderson, *J.*, 1925, **127**, 1944).

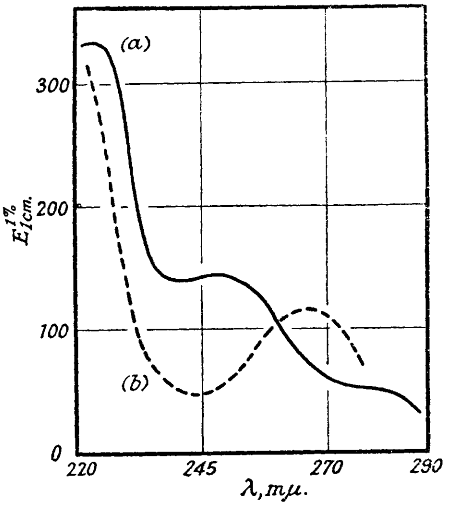
The problem of the structure of *iso*cadinene was obviously one to which the absorption spectrum method might be applied with some hope of success, and we have therefore prepared samples of *iso*cadinene from cade oil by several methods for spectroscopic study. The physical constants of the preparations are in close agreement with those recorded by earlier workers (see Table).

iso*Cadinene samples from oil of cade and from cadinene.*

Preparation.	B. p.	$n_D^{20°}$.	$d_4^{20°}$.	λ max. (A.).	ε max.
A. Ether as solvent	112—115°/5 mm. ...	1·5168	0·9184	2250	10,200
				2470	6,160
B. Ether as solvent	121—123/8 mm.	1·5147	0·9186	2240	10,080
				2450	3,690
C. Acetic acid as solvent	113—118/5 mm.	1·5153	0·9162	2240	9,940
				2470	5,350
D. From cadinene	100—104/1·2 mm.	1·5157	0·9220	> 2200	6,500
				2650	2,400

The absorption spectrum of a typical sample of *iso*cadinene is shown in Fig. 1, and since compounds containing even several unconjugated ethylene linkages do not normally show absorption maxima at wave-lengths longer than about 2000 A. it can be inferred at once from the observed light-absorption data that *iso*cadinene contains a conjugated diene system. Further, the absorption spectra of a wide range of dienes have been examined (Booker, Evans, and Gillam, *J.*, 1940, 1453) and these all showed only one broad absorption band (discounting the submaxima found exceptionally, *e.g.*, ergosterol). Now since *iso*cadinene is the only diene to exhibit *two* broad absorption bands, and since these are found to vary slightly in relative intensity from sample to sample, the inference is that this hydrocarbon is heterogeneous. To confirm this it was necessary to find a method of separation of the components. Careful fractional distillation in a vacuum was tried without much success except the production of slight variations in the relative intensities of the two bands, so recourse was had to chromatography.

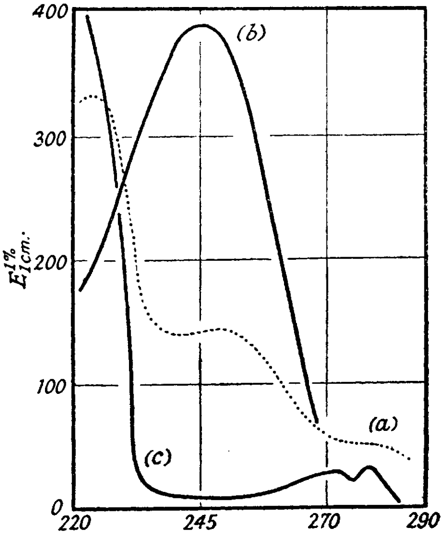
FIG. 1.



Absorption spectra, in alcohol, of :

(a) *a typical* iso*cadinene from oil of cade ;*
(b) *a less typical sample prepared from cadinene.*

FIG. 2.



Absorption spectra, in alcohol, of typical iso*cadinene fractions :*

(a) *original* iso*cadinene ;*
(b) *the* 2450A.*-absorbing component ;*
(c) *the other main fraction.*

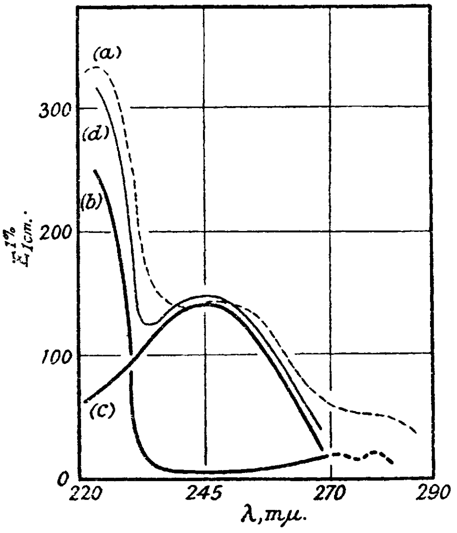
Various samples of *iso*cadinene were adsorbed on alumina from benzene-free hexane or light petroleum and washed with the same solvent. The washings were collected arbitrarily into fractions, the solvent removed under reduced pressure, and the resulting solutes examined, using the absorption spectrum as the first criterion. Typical results are given in the experimental section, and it is quite clear that what has been previously called " *iso*cadinene " is in fact a mixture. Evidence has been obtained of two main components absorbing light maximally at 2450 A. and at $<$ 2200 A. (cf. Fig. 2). There is also a third component having a characteristically-shaped absorption curve with two submaxima at 2710 and 2785 A. respectively (cf. Fig. 2). This is only a minor constituent and, judging from the location of the absorption bands, is probably a more unsaturated impurity.

Let us consider the component absorbing maximally at 2450 A. Fractions containing this compound were obtained repeatedly and were bulked for examination since only small quantities of labile liquid were obtained at each fractionation (cf. Experimental). Molecular weight determination by the micro-Rast method gave a value of 205 which agrees with a hexahydrocadalene (calc., 204). Microhydrogenation shows the compound to contain two ethylene linkages, whilst the location and intensity of the absorption band (λ max. 2450 A., $\varepsilon > 5000$) proves that these are conjugated. Since absorption data on dienes of known structure are available (Booker *et al.*, *loc. cit.*), and since it is known that dienes having two double bonds in one ring absorb between 2600 and 2820 A. whilst those having two such bonds between two rings have their maxima situated between 2350 and 2480 A., it is very probable that this component (λ max. 2450 A.) is of the latter type. Further, we were unable to detect either acetone or formaldehyde on ozonisation which would preclude an *exo*cyclic double bond and indirectly add support to the suggestion that both double bonds form parts of separate rings. There appear to be six possible hexahydrocadalenes that will fit these facts, but we were unable to obtain sufficient of this particular component to carry out degradative experiments.

If we assume that Woodward's method of calculating the location of the absorption bands of conjugated dienes (*J. Amer. Chem. Soc.*, 1942, **64**, 72) is applicable to bicyclic dienes, the calculated absorption maxima of these hexahydrocadalenes all fall between 2400 and 2500 A. which compares well with our observed value of 2450 A.

The other component of " *iso*cadinene " is responsible for the band at 2200—2240 A. in the original material, but on purification by chromatographic separation this moves to < 2200 A. The ratio of intensities of the two bands at 2200 and 2450 A., respectively, in the starting material was 2·3, but it was found possible to alter the relative concentrations of the two components so that this value went up to as much as 13·0 (cf. Experimental). Micro-Rast determination of molecular weight gave a value of 209, and the light-absorption data would be explained by the presence of an acyclic diene of the mono- or di-substituted type (known range 2170—2280 A). Alternatively, the absorption might be due to a compound with one or even two substituted ethylene linkages not in conjugation, possibly mixed with a conjugated acyclic diene.

FIG. 3.



Summation of the absorption spectra of the two main components :

(a) *original* iso*cadinene ;*
(b), (c) *contributions made by separated components ;*
(d) *summation curve of* 64% (b) *and* 36% (c).

The tentative explanation we prefer is that " *iso*cadinene " is a mixture of a conjugated diene and a substituted ethylenic compound, the former having an absorption band at 2450 A. and the latter a band at < 2200 A. Fig. 3 shows the result of a hypothetical addition of the two main components shown in Fig. 2 in the proportions of 36% of the 2450 A. component and 64% of the 2220 A. component. The curve for the resultant mixture is somewhat similar to that of a number of typical samples of " *iso*cadinene " having constants closely in agreement with those found by Henderson and J. M. Robertson. Such a mixture in about these proportions would also account for the figure of 1·2 double bonds per molecule found for the original sample of *iso*cadinene. This explanation tacitly assumes that the two bands at 2710 and 2785 A. are due to a third, probably more unsaturated, impurity.

The samples of *iso*cadinene from cade oil which have been discussed above (A, B, and C, Table, p. 1306) are typical of others examined, but on occasion, especially in samples prepared from cadinene rather than cade oil, the usual absorption band at 2450 A. is displaced to longer wavelengths, usually about 2650 A. (cf. D, Table, p. 1306). Such a sample has not been subjected to chromatographic separation, but it would seem probable that when cadinene is isomerised to *iso*cadinene several different arrangements of the conjugated system are possible, and, although the most usual isomer has its two ethylene linkages distributed between two rings, the compound responsible for the 2650 A. band is probably an isomer having the two unsaturated linkages in the same ring as in Ruzicka and Capato's compound (III). This is based on the known light-absorption data on α-phellandrene (λ max. 2630 A.) and similar compounds (for details cf. Booker *et al.*, *loc. cit.*).

Experimental.

Preparation of " iso*Cadinene* ".—(*a*) An appropriate fraction of cade oil was dissolved in acetic acid and treated with hydrogen chloride. After removal of the crystalline cadinene hydrochloride, the oily hydrochloride was worked up as described by Henderson and A. Robertson (*J.*, 1924, **125**, 1922) to give *iso*cadinene of which the constants are given in the table (p. 1306).

*iso*Cadinene regenerated from the liquid hydrochloride obtained by passing hydrogen chloride into an ethereal solution of the cade oil fraction had similar constants (see table).

(*b*) Cadinene (20 g.) (regenerated from the hydrochloride, m. p. 118—119°), having b. p. 104—106°/2 mm., $n_D^{20^\circ}$ 1·5069, was treated with glacial acetic acid (1000 g.) and sulphuric acid (30%, 40 ml.) as described by Henderson and A. Robertson (*loc. cit.*). The product (15·5 g.) was fractionated to give *iso*cadinene. The constants of these samples are summarised earlier.

Attempts to separate iso*Cadinene into Constituents.*—Attempts to separate "*iso*cadinene" into different constituents by fractional distillation were unsuccessful. A solution of *iso*cadinene (10 g.) and maleic anhydride (5 g.) in benzene (25 ml.) was heated on the water-bath under reflux for 24 hours, after which the very small quantity of crystalline material which had separated on cooling (0·05 g.) was removed. The benzene was washed until neutral, and the recovered oil distilled to recover *iso*cadinene (7·8 g.), b. p. 106—120°/2·5 mm., and a second product (1·8 g.), b. p. 175—190°/2 mm., which was not further examined. The recovered oil was washed and steam-distilled to give recovered *iso*cadinene, b. p. 120—122°/5 mm., $n_D^{20^\circ}$ 1·5147, $d_{4^\circ}^{20^\circ}$ 0·9176, λ max. 2230 A., ε = 14,000, inflexion near 2520 A., ε = 1840. When *iso*cadinene (5·6 g.) prepared from cadinene was treated in this manner the recovered *iso*cadinene (4·7 g.) had b. p. 101°/1 mm., $d_{4^\circ}^{20^\circ}$ 0·9184, ε at 2200 A. (no band) = 10,300; clearly separated band 2675 A., ε = 1430.

In other experiments of which the following is typical an appropriate cade oil fraction (800 g.), b. p. 123—142°/11 mm., $n_D^{20^\circ}$ 1·5176, was dissolved in ether and treated with dry hydrogen chloride for 5 hours. After standing overnight the ether was removed by distillation and the residue refrigerated. The crystalline cadinene hydrochloride (86 g.) was removed, the filtrate being distilled under reduced pressure to give fractions as follows:

Fraction.	B. p./2 mm.	Wt. (g.).	Cl, %.
(1)	105—109°	630	2·2
(2)	109—112	60	3·5
Residue	—	190	15·5

Fraction (1) was rejected. The residue on cooling deposited more cadinene hydrochloride (12 g.), and the filtrate (Found: Cl, 8·9%) was bulked with fraction (2); this mixture was dissolved in dry ether, hydrogen chloride passed in for two 5-hour periods, and then excess of ether and hydrogen chloride distilled off under reduced pressure to give a product which crystallised on refrigeration. The crystalline cadinene hydrochloride was removed, the filtrate (Found: Cl, 13·2%) was again treated with hydrogen chloride as before, and a further 8 g. of crystals were removed. This filtrate (220 g.) (Found: Cl, 13·1%) was repeatedly extracted with alcohol (90% v/v), using 100 g. of filtrate and extracting 4 times with 25 ml. of alcohol, to give an insoluble portion (160 g.) (Found: Cl, 12·6. Calc. for $C_{15}H_{26}Cl_2$: Cl, 25·6%. Calc. for $C_{15}H_{25}Cl$: Cl, 15·3%) and a soluble portion (35 g.) (Found: Cl, 10·0%). The alcohol-insoluble portion (60 g.) on dehydrochlorination with sodium acetate and acetic acid gave a product (54 g.) of which the main constituent (A) (14·2 g.) obtained by vigorous fractionation had b. p. 86—90/0·6 mm., $d_{4^\circ}^{20^\circ}$ 0·9218, $n_D^{20^\circ}$ 1·5140, $\alpha_D^{20^\circ}$ − 47·9°, λ max. 2220 A., ε = 6420, inflexion 2490 A., ε = 2620 (Found: C, 86·9; H, 11·3. Calc. for $C_{15}H_{24}$: C, 88·2; H, 11·8%). The alcohol-soluble portion (34 g.) on similar treatment gave a product (7·8 g.) having b. p. 89—92°/0·7 mm., $n_D^{20^\circ}$ 1·5167, $\alpha_D^{20^\circ}$ − 40·5°, $d_{4^\circ}^{20^\circ}$ 0·9263, λ max. 2220 A., ε = 7160, inflexion 2450 A., ε = 3620 (Found: C, 78·7; H, 11·4%); this was not further examined.

The (A) above (1·098 g.) was subjected to chromatographic adsorption on activated alumina in light petroleum, and the chromatogram developed with the same solvent, 25 ml. fractions being collected. Approximately 75% of the sample was recovered from fractions 8 to 11 as follows:

Fraction.	Wt. (g.).	λ max. (A.).	$E_{1\,\text{cm.}}^{1\%}$.	$E_{1\,\text{cm.}}^{1\%}$ 2220 A. / $E_{1\,\text{cm.}}^{1\%}$ 2450 A.
8	0·595	2450, 2220	153, 211	1·4
9	0·285	(2450), 2220	136, 281	2·1
10	0·3115	(2470), 2220	125, 315	2·5
11	0·141	(2470), 2350	123, 376	3·1
Original sample 52/6	—	(2470), 2240	144, 333	2·3

The 2450 A. *component.* By carrying out a series of chromatograms, bulking suitable fractions from each, and readsorbing them on a fresh column the following fractions were amongst those produced (Moss, Thesis, Manchester University, 1947).

Fraction.	Wt. (mg.).	λ max. (A.).	$E_{1\,\text{cm.}}^{1\%}$.	$E_{1\,\text{cm.}}^{1\%}$ 2220 A. / $E_{1\,\text{cm.}}^{1\%}$ 2450 A.
IV, 6	6·5	2220, 2450	144, 249	0·6
IV, 8	9·5	2220, 2450	134, 211	0·6
V, 9	3·6	2220, 2440	111, 133	0·8
V, 10	6·6	2220, 2450	118, 221	0·5
V, 11	10·3	2220, 2450	129, 210	0·6
V, 12	18·8	2220, 2450	147, 210	0·7

Although there seems little doubt as to the location (2450 ± 10 A.) of the absorption band, the intensity figures are probably very low, since these dienes are susceptible to oxidation, and since further it was difficult to remove the last traces of solvent even in a vacuum over silica gel. The fractions showed average *M* (micro-Rast), 205; calc. for $C_{15}H_{24}$: 204. Microhydrogenation of fraction IV, 6 gave a value $\vDash$ 1·8 (*M* taken, 204) whereas the original material before chromatography had $\vDash$ 1·2 (*M* taken, 204).

The component absorbing near 2200 A. The following fractions are typical of those enriched in the component absorbing maximally near 2220 A.

Fraction.	Wt. (g.).	λ max. (A.).*	$E^{1\%}_{1\,\text{cm.}}$.	$E^{1\%}_{1\,\text{cm.}}$ 2220 A. / $E^{1\%}_{1\,\text{cm.}}$ 2450 A.
II, 11	0·141	2235, (2470)	376, 123	3·1
V, 14	0·2336	2220, (2450)	274, 36	7·7
VI, 9	0·070	2220, (2490)	77, 7	11

* Wave-lengths in parentheses indicate inflexions rather than clearly separated maxima.

For the fraction richest in the 2220 A. component, micro-Rast determination gave *M*, 209.

Other chromatographic separations of the original *iso*cadinene carried out in air and in an atmosphere of nitrogen confirmed, in general, the above results, but an absorption curve with a principal maximum at a shorter wave-length than 2220 A. and two subsidiary maxima at 2710 A. and 2785 A. was obtained. The last two bands were also shown to be present in the absorption curve of the original sample. The following fractions are typical of chromatograms obtained in later experiments.

Fraction.	Wt (g.).	% of starting material.	λ max. (A.).	$E^{1\%}_{1\,\text{cm.}}$.	$E^{1\%}_{1\,\text{cm.}}$ 2240 A. / $E^{1\%}_{1\,\text{cm.}}$ 2450 A.
7	0·1207	12	(2240), (2450), 2800	193, 20·0, 13·0	9·5
8	0·0817	8	(2240), (2450), 2710, 2785	240, 9·1, 21, 22·5	10·7
9	0·0641	6	(2240), 2710, 2785	270, 24·6, 26·5	10·2
10	0·0450	4½	2240, 2710, 2785	260, 20·5, 22·0	11·8
11	0·0736	7	2240, 2710, 2785	230, 17·5	13
12 Eluted with petrol–alcohol	0·091	7½	2785	—	—

Absorption spectra were measured in alcoholic solution on a Hilger E3 quartz spectrograph in conjunction with a Spekker photometer.

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