143. *Observations on the Absorption Spectra of Terpenoid Compounds. Part I.* " iso*Thujone.*"

By A. E. Gillam and T. F. West.

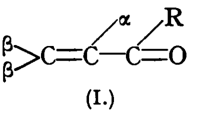
The chemical evidence adduced by Wallach indicates that the mixture of ketones produced by the action of sulphuric acid on thujone consists mainly of " *iso*thujone " (*dl*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone), the optically active form of which has since been prepared by Short and Read (J., 1939, 1040). Although the absorption spectrum of the *dl*-ketone clearly indicates the presence of the C=C–C=O chromophoric group, yet the location of the absorption maximum is inconsistent with the presence of an αββ-trisubstituted chromophoric system, and the observed data can apparently only be explained by the presence of a disubstituted group unless it be assumed that " *iso*thujone " is exceptional among αβ-unsaturated ketones. The absorption of a specimen of *l*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone derived from *d*-sabinol (Short and Read, *loc. cit.*) shows even greater divergence from the value of $\lambda_{max.}$ expected on the basis of the accepted structure.

The action of sulphuric acid on thujone (II) has been investigated by Wallach (*Annalen*, 1895, **286**, 101) and by Haller (*Compt. rend.*, 1905, **140**, 162) and the former showed that the principal product was the *dl*-form of an unsaturated ketone (III) to which he gave the name " *iso*thujone," although Short and Read (J., 1938, 2016) have since pointed out that this should be named systematically as a *cyclo*pentenone derivative. According to Wallach (*Ber.*, 1895, **28**, 1958; *Annalen*, 1902, **323**, 324), when thujone was treated with sulphuric acid, the mixture of ketones thereby produced gave a crude semicarbazone, m. p. 184—192°, which could be separated into an α-semicarbazone, m. p. 208—209°, and a β-semicarbazone, m. p. 184—185°, both of which regenerated *dl*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone. Although identical melting points were given for each of these semicarbazones in both references, no details of the method of separation appear to have been recorded.

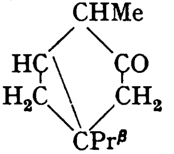
The crude semicarbazone obtained by us, from a ketone mixture having appropriate constants, has a melting range similar to that recorded by Wallach, but despite an exhaustive examination (see Experimental), we could only isolate, in addition to the semicarbazone of *d*-carvotanacetone, one semicarbazone having m. p. 207—208°. It may be significant that Wallach later (*Annalen*, 1915, **408**, 163) recorded the difficulty of obtaining uniform " *iso*thujone " free from carvotanacetone, and that Haller (*loc. cit.*) did not describe the preparation of derivatives for identification.

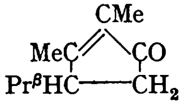
It has been suggested (Simonsen, " The Terpenes," I, p. 297) that the carvotanacetone found in thuja oil (Wallach, *Annalen*, 1893, **275**, 182) may have been formed from thujone during its isolation, but it was evident from the absorption spectrum that the *d*-thujone forming the basis of the present experiments was free from this ketone before treatment with sulphuric acid. The identity of the *dl*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone with the " *iso*thujone " described by Wallach was confirmed by the preparation of the oxime, m. p. 119—120° (*Ber.*, 1895; *Annalen*, 1915, *locc. cit.*).

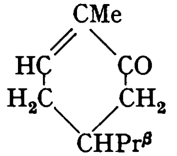
The absorption spectra of αβ-unsaturated ketones are so characteristic that they have been widely used to detect the presence of the system C=C–C=O in a variety of compounds. Woodward (*J. Amer. Chem. Soc.*, **1941**, **63**, 1123) has recently extended the application of absorption-spectra data in this connection by showing that the location of the short-wave band of high intensity in this type of compound varies with the substitution of the C=C–C=O chromophore in a very regular way. For instance, if the chromophoric grouping be written as in (I), some fifty different alkyl-substituted αβ-unsaturated ketones fall clearly into three classes which are easily differentiated by the location of the " ethylene " band in the absorption spectrum, and moreover the classes do not overlap.


(I.)

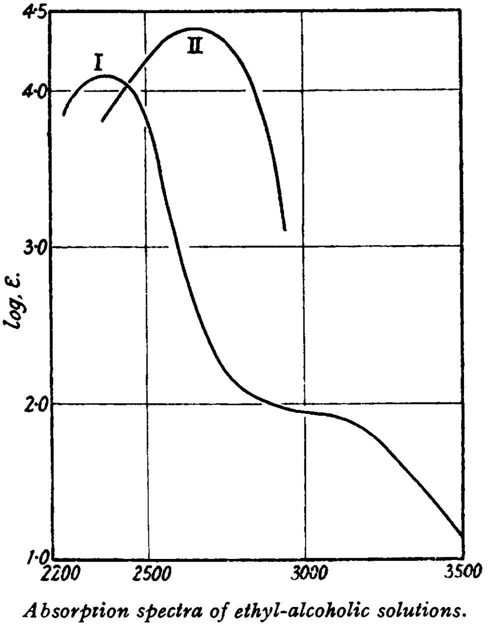
The generalisation is discussed more fully in the following paper, which deals primarily with absorption spectra. Here we deal only with " *iso*thujone," the absorption spectrum of which is shown in the figure. The particular specimen used for this purpose was a homogeneous fraction obtained from the crude " *iso*thujone " by the method detailed in Table I. It was regenerated from the purified semicarbazone (m. p. 207—208°) and, following Read's nomenclature, should be named *dl*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone (III).


(II; Thujone.)


(III; " *iso*Thujone.")


(IV; Carvotanacetone.)

The location of the absorption band at 2375 A. classifies *iso*thujone as a disubstituted αβ-unsaturated ketone, whereas the formula generally accepted (III) involves trisubstitution of the chromophoric grouping. Hence, either *iso*thujone is exceptional among αβ-unsaturated ketones in that its main absorption maximum is displaced to shorter wave-lengths than would be expected from our generalised experience, or the accepted formula is incorrect. In order to accord with Woodward's generalisation the *iso*thujone molecule should contain a disubstituted chromophoric grouping. This is supported by the similarity between the light-absorption data on *iso*thujone and on compounds known to contain the disubstituted C=C–C=O structure (cf. Table II). It should be noted that a six-atom ring structure is among the possible formulæ that would meet the light-absorption data although such a formula cannot apparently be made to fit the chemical evidence adduced by Wallach and his co-workers.



Absorption spectra of ethyl-alcoholic solutions.
I. iso*Thujone.*
II. iso*Thujone semicarbazone.*

Through the kindness of Professor J. Read, F.R.S., we were able to examine a specimen of *l*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenone (III), which is the optically active form of Wallach's *iso*thujone but is derived from a completely different source, *i.e.*, *d*-sabinol. By hydrogenation in the presence of colloidal palladium, this alcohol gives *d*-2 : 3-dimethyl-4-*iso*propyl-Δ^2-*cyclo*pentenol, which is oxidised by Beckmann's chromic acid mixture to the *l*-ketone (Short and Read, J., 1939, 1043). The absorption spectrum of this compound showed the usual two maxima, at 2310 A. (ε = 6180) and 3100 A. (ε = 35), to be expected from an αβ-unsaturated ketone.

Comparison of these data with the spectrum given by *iso*thujone at once raises two points. First, these two compounds are sufficiently different in the locations of the main absorption maxima as to raise considerable doubts as to their identity, since stereoisomerides (or *l*- and *dl*-compounds) usually have identical absorption spectra. Secondly, this *l*-pentenone is even more anomalous than the *dl*-*iso*thujone in that its absorption band is displaced to shorter wave-lengths ($\lambda_{max.}$ 2310 A.), *i.e.*, even further away from the value (2540 ± 50 A.) to be expected of the trisubstituted αβ-unsaturated ketone represented by the five-membered ring formula (III).

TABLE I.

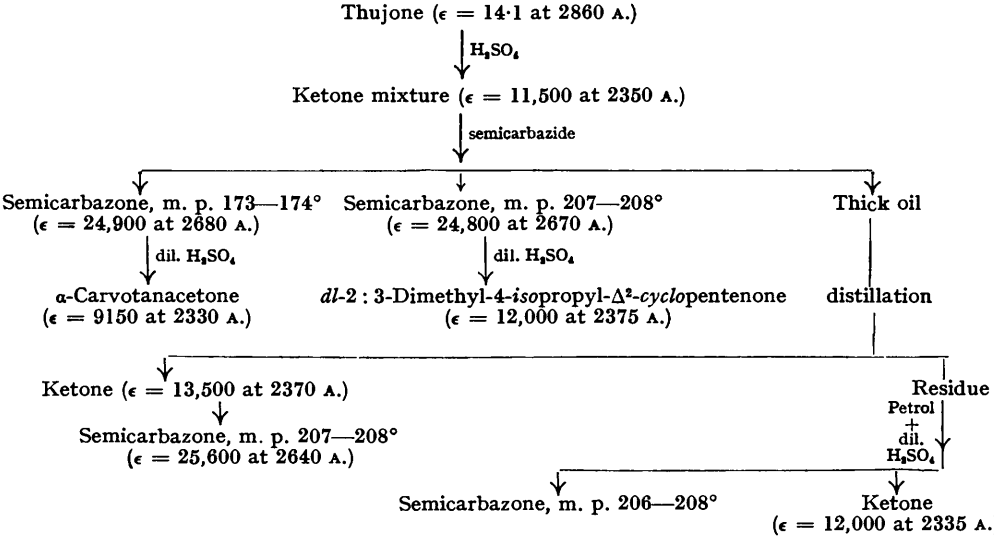


TABLE II.

Absorption-spectra data for solutions in alcohol.

	K-Band.		*R*-Band.	
	$\lambda_{max.}$	$\epsilon_{max.}$	$\lambda_{max.}$	$\epsilon_{max.}$
Carvone[1]	2353	19,050	3175	42
d-Carvotanacetone (IV)	2330	9,150	not measured	
*iso*Thujone (III)	2375	12,000	(3100)	80
l-2 : 3-Dimethyl-4-*iso*propyl-Δ²-*cyclo*pentenone	2310	6,180	3100	35
1-Methyl*cyclo*hexen-3-one[2]	2350	12,930	3120	46
Thujone (II)	—	—	2860	14·1
*iso*Thujone semicarbazone	2670	24,800	—	—
Carvotanacetone semicarbazone	2680	24,900	—	—

[1] Data by Cooke and Macbeth (J., 1938, 1408). [2] Evans and Gillam (following paper).

EXPERIMENTAL.

(Analyses by Drs. Weiler and Strauss, Oxford.)

Preparation of Thujone.—After a number of experiments the thujone was satisfactorily extracted from tansy oil as follows. The oil (150 g.), showing 72% w/w of a ketone $C_{10}H_{16}O$ by the hydroxylamine hydrochloride method, was added to a saturated sodium bisulphite–sulphite solution (150 ml.) and 50 ml. of industrial alcohol, and this mixture shaken during 9 hours. The bisulphite cake was sucked dry, and washed twice with a mixture of alcohol (2 parts) and ether (3 parts). This cake (148 g.) was added to a 20% solution of sodium hydroxide (1 l.) and ether (100 ml.), and the mixture stirred mechanically for 20 mins. The ethereal solution was separated, the alkaline solution again extracted with ether, and the bulked extracts dried with sodium sulphate. After removal of solvent, the thujone (54 g.) distilled at 76—80°/3 mm., and had $n_D^{15°}$ 1·4550, $d_{15°}^{15°}$ 0·9186, α_D + 70·8°. The ketone showed maximum absorption at 2860 A. (ε = 14·1) typical of a saturated ketone. There was therefore no evidence for the formation of carvotanacetone during its isolation.

Action of Sulphuric Acid on Thujone.—In a typical experiment sulphuric acid (60 g.) was cooled to 0°, and thujone (20 g.) added slowly with stirring below 5° (cf. Haller, *Compt. rend.*, 1905, **140**, 1630). The mixture was at once poured into ice water (1 l.), and the oil extracted with ether. The ethereal solution was washed with water until neutral, dried with sodium sulphate, the solvent removed, and the oil distilled. The main fraction (15 g.) had b. p. 87—90°/3 mm., 228—230°/751 mm., $n_D^{22°}$ 1·4807, $d_{15°}^{15°}$ 0·9263, α_D + 17·6°. The absorption spectrum consisted of a band of high intensity at 2375 A. (ε = 12,000) and a subsidiary inflexion near 3100 A. (ε = 80), the two together being characteristic of αβ-unsaturated ketones.

Examination of the Mixed Semicarbazone.—Semicarbazide hydrochloride (16·5 g.) and crystalline sodium acetate (22·5 g.) were dissolved in water (22 ml.), and 37 ml. of alcohol added. The warm solution was added to the ketone mixture, prepared from *d*-thujone as described above (22·5 g.), dissolved in 75% alcohol (75 ml.). After standing overnight at room temperature, the solution was cooled until no further solid material separated. These crystals (8 g.) had m. p. 186—191°, raised by two recrystallisations from methyl alcohol to 207—208° (decomp.) (Found: N, 19·8. Calc. for $C_{11}H_{19}ON_3$: N, 20·1%). The *dl*-2 : 3-dimethyl-4-*iso*propyl-Δ²-*cyclo*pentenone regenerated from this semicarbazone by steam-distillation in the presence of dilute sulphuric acid had b. p. 87—88°/3 mm., $n_D^{20°}$ 1·4839, $d_{15°}^{20°}$ 0·9285, α_D ± 0° (*c*, 6·5 in alcohol) (Found: C, 78·2; H, 10·6. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·5%). The semicarbazone showed maximum absorption at 2670 A. (ε = 24,800) and the regenerated ketone showed ε = 12,000 at 2375 A. (see figure). The oxime had m. p. 119° (Wallach, *Ber.*, 1895, **28**, 1958).

After removal of the crude semicarbazone, the filtrate was poured into water and extracted with ether. The oil thus recovered was diluted with light petroleum (300 ml.), and the solution cooled for some days until no further crystals separated. These crystals (3·2 g.) had m. p. 164—166°, raised by repeated crystallisation from methyl alcohol to 173—174° (decomp.) (Simonsen and Rau, J., 1922, **121**, 876) (Found: N, 19·6. Calc. for $C_{11}H_{19}ON_3$: N, 20·1%). The *d*-carvotanacetone regenerated from this semicarbazone had b. p. 86—87°/3 mm., $n_D^{20°}$ 1·4797, $d_{15°}^{18°}$ 0·943, α_D + 36° (*c*, 2·45 in alcohol) (Found: C, 78·8; H, 10·6. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·5%). The semicarbazone showed maximum absorption at 2680 A. (ε = 24,900) and the regenerated ketone at 2330 A. (ε = 9000).

Removal of the light petroleum from the filtrate produced a viscous yellow oil which gave by vacuum distillation 10 g. of oil (b. p. 85—97°/3 mm.). This was shaken with 10% sulphuric acid and redistilled to give an oil having b. p. 86—88°/2 mm., $n_D^{20°}$ 1·4840, $d_{15°}^{15°}$ 0·920, α_D + 8·6° (Found: C, 79·4; H, 10·8. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·5%). The semicarbazone had m. p. 207—208°, and the oxime m. p. 119—120° (Found: N, 8·2. Calc. for $C_{10}H_{17}ON$: N, 8·4%). The ketone displayed maximum absorption at 2370 A. (ε = 13,500) and an inflexion (ε = 383) at 3020 A., probably largely due to an impurity. The semicarbazone had $\varepsilon_{max.}$ 25,600 at 2640 A.

The residue left after distillation of the above fraction was dissolved in benzene–light petroleum, and after long standing at 0° the crystals (0·6 g.) had m. p. 168—172°, raised to 206—208° by repeated recrystallisation from methyl alcohol, not depressed by admixture with *dl*-2 : 3-dimethyl-4-*iso*propyl-Δ²-*cyclo*pentenone semicarbazone.

After removal of solvent from the filtrate, 10% sulphuric acid (60 ml.) was added to the residue, the mixture steam-distilled, and the oil from the distillate worked up. The product (4 g.) had b. p. 87—90°/3 mm., $n_D^{19°}$ 1·4802, $d_{15°}^{20°}$ 0·925, α_D + 7° (Found: C, 78·7; H, 10·6. Calc. for $C_{10}H_{16}O$: C, 78·9; H, 10·5%). It showed maximum absorption at 2335 A. (ε = 12,000) and an inflection near 3080 A. (ε = 86). It was not possible to obtain a crystalline oxime, and the semicarbazone, in spite of repeated crystallisation, was obviously a mixture, since the crystals sintered at 130°, began to darken at 145°, and finally melted at 160—161°.

l-2 : 3-*Dimethyl*-4-iso*propyl*-Δ²-cyclo*pentenone* (cf. Read and Short, J., 1939, *loc. cit.*).—Prof. Read's specimen of this compound had b. p. 89°/13 mm., $\alpha_D^{19°}$ −12·72°. The solution in alcohol showed $\lambda_{max.}$ 2310 (ε = 6180) and 3100 A. (ε = 35).

Determinations of absorption spectra were made on a Hilger E_3 quartz spectrograph in conjunction with a Spekker photometer, standard methods being used.

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