152. *α-Cyperone, a Sesquiterpene Ketone from the Oil of* Cyperus rotundus.

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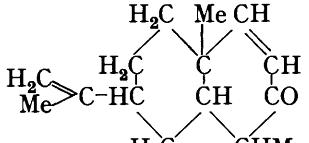
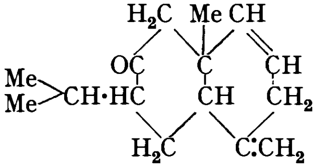
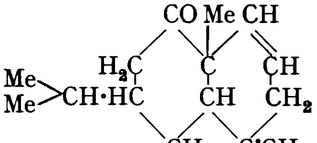
A. E. Gillam.

Although the oil from the tubers of *Cyperus rotundus* has been frequently investigated, it is only recently (Hegde and Rao, *J. Soc. Chem. Ind.*, 1935, **54**, 387T) that the higher-boiling fractions have been shown to consist largely of sesquiterpene ketones. The main constituent, *α-cyperone*, can be purified readily through its *semicarbazone*, m. p. 216°, and has the composition $C_{15}H_{22}O$. It is dicyclic and contains two ethylenic linkages, yielding on catalytic hydrogenation *tetrahydro-α-cyperone.* Like eremophilone (J., 1932, 2744), it is a derivative of eudalene, since *dihydro-α-cyperol* yields this hydrocarbon on dehydrogenation with selenium.

It will now be shown that α-cyperone must be represented by (I), although its somewhat anomalous reactions led us originally to the erroneous conclusion that it had probably either formula (II) or (III) (compare J., 1935, 785).


(I.)


(II.)

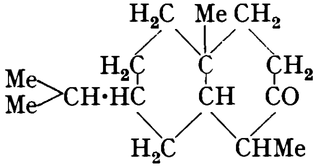

(III.)

It was readily proved that one of the ethylenic linkages must be present as an exocyclic methylene group. Dihydro-α-cyperol, obtained by the reduction of α-cyperone with sodium and alcohol, whereby the keto-group and one ethylenic linkage were reduced simultaneously, on oxidation with ozone yielded formaldehyde and a ketonic alcohol, from which, by further oxidation with chromic acid, a colourless diketone, $C_{14}H_{22}O_2$, was prepared. Since neither the keto-alcohol nor the diketone gave bromoform with sodium hypobromite or iodoform with Fuson's reagent (Fuson and Tullock, *J. Amer. Chem. Soc.*, 1934, **56**, 1638), it appeared unlikely that the parent alcohol could contain an *iso*propenyl group, a deduction which seemed to receive support from the absence of acetone from the oxidation products. It was assumed, therefore, that the methylene group was attached directly to the ring as in (II) or (III), but this assumption became doubtful when it was found that *dihydro-α-cyperyl* 3 : 5-*dinitrobenzoate* gave on ozonolysis a *ketone*, $C_{21}H_{26}O_7N_2$, m. p. 148—149°, from which iodoform was obtained on oxidation with Fuson's reagent.

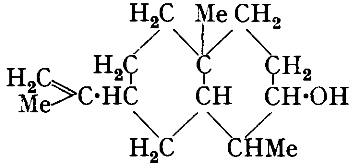
In view of these contradictory results it became necessary to establish directly the position of the carbonyl group. This was effected by treating tetrahydro-α-cyperone with methylmagnesium iodide and dehydrogenating the alcohol so obtained with selenium, whereby 1 : 2-dimethyl-7-*iso*propylnaphthalene was formed. The identity of this hydrocarbon was proved by a comparison of the *picrate*, m. p. 92—93°, and the s.-*trinitrobenzene* derivative, m. p. 108—110°, with synthetic specimens.

Since tetrahydro-α-cyperone was thus rigidly proved to be 1 : 10-dimethyl-7-*iso*propyldecal-2-one (IV), it followed that dihydro-α-cyperol must be the related *iso*propenyl derivative (V), this structure alone explaining the formation of the ketone (VI) which would yield iodoform on oxidation with Fuson's reagent. The only alternative formula containing a methylene group (VII) is impossible, since an ethylenic linkage in this position would have been in the αβ-position to the original carbonyl group and would, therefore, have been reduced by sodium and alcohol.

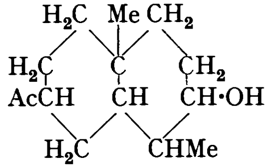
(IV.)



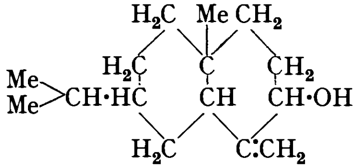
(V.)



(VI.)



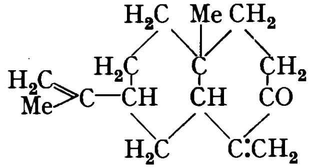
(VII.)

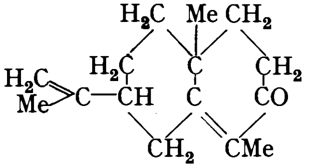


It is now only necessary to ascertain the position of the second ethylenic linkage. Here again it was found that the evidence was conflicting. The reduction of this linkage with sodium and alcohol implies either that the two ethylenic linkages are conjugated with each other or that the carbonyl group has an ethylenic linkage in the αβ-position. On the one hand, the conjugation of the two ethylenic linkages is rendered highly improbable by the fact that the hydrocarbon *α-cyperene*, obtained from α-cyperone semicarbazone by the Wolff–Kishner reaction, could not be reduced by sodium in either ethyl or amyl alcohol solution. On the other hand, no direct evidence of conjugation with the carbonyl group was forthcoming. The ketone does not yield a derivative with hydrogen sulphide in the presence of alcoholic ammonia, or react with hydrogen cyanide (Lapworth and Clarke, J., 1906, **89**, 1872), and with hydrogen peroxide in alkaline solution no oxide is formed. In the last reaction, the greater part of the ketone was recovered as β-*cyperone* (see p. 674); a small quantity of a crystalline *keto-acid*, $C_{13}H_{20}O_3$, m. p. 112°, was, however, formed, the constitution of which is discussed on p. 669. Nevertheless, we conclude that conjugation with the carbonyl group is the more likely alternative, since negative results with the tests for an αβ-ethylenic linkage enumerated above are of doubtful diagnostic value. This conclusion is supported by a study of the absorption spectrum of α-cyperone (p. 676), and by the apparently abnormal formation of a hydroxymethylene derivative, discussed below, and it is in harmony with the course of the oxidation of the ketone and its derivatives.

This conclusion being accepted, α-cyperone must be represented by either (I), (VIII), or (IX). A study of the ozonolysis products of α-cyperone and of its semicarbazone showed (I) to be correct. The former yields, in addition to formaldehyde, a liquid dibasic keto-acid, $C_{13}H_{20}O_5$, the *dimethyl* ester of which was characterised by its *semicarbazone*, m. p. 245—246°. This acid must have the structure (XI), having been formed from the primary product of the oxidation (X) which, being an α-keto-acid, would be readily oxidised by the hydrogen peroxide generated during the decomposition of the ozonide. The formation of this acid excludes formulæ (VIII) and (IX).

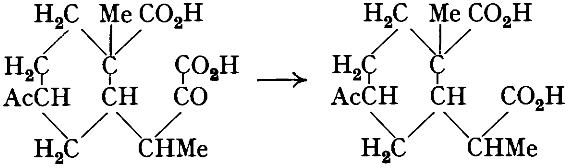
(VIII.)





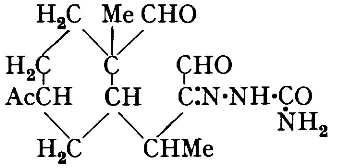
(IX.)

(X.) (XI.)

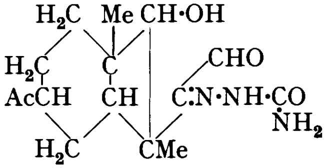


Ozonolysis of α-cyperone semicarbazone gave a *semicarbazone*, $C_{15}H_{23}O_4N_3$, m. p. 185—187°. To this substance, which is a powerful reducing agent, we assign either formula (XII) or (XIII), its formation providing further proof that only one of the ethylenic linkages in α-cyperone is exocyclic.

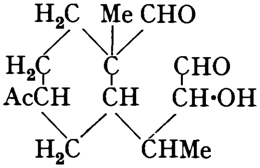
During the ozonolysis of an impure specimen of dihydro-α-cyperol, which evidently contained some α-cyperol, the related alcohol (XIV) was formed; it was isolated as a *di-* or *tri-phenylsemicarbazone*, m. p. 222—223°.



(XII.)

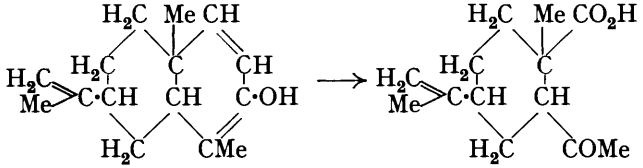


(XIII.)

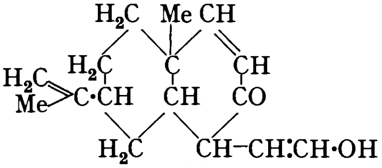


(XIV.)

It was mentioned above that by the oxidation of α-cyperone with hydrogen peroxide in alkaline solution a keto-acid, $C_{13}H_{20}O_3$, was obtained. There can be little doubt that this acid is *6-acetyl-1-methyl-4-*iso*propenyl*cyclo*hexane-1-carboxylic acid* (XVI), having been formed by the oxidation of the enolic form (XV) of the ketone.



(XV.) (XVI.)



(XVII.)

Although the reactions outlined above are in full accord with the structure (I) assigned to α-cyperone, a serious difficulty arises from the fact that the ketone gives an excellent yield of a liquid hydroxymethylene derivative, 2 : *4-dinitrophenylhydrazone*, m. p. 159—160°, a reaction usually regarded as providing a sure indication of the presence of the group $-CH_2 \cdot CO-$. This group is not present in formula (I). By catalytic hydrogenation of the hydroxymethylene derivative, which was slow and incomplete, followed by reduction with sodium and alcohol, a substance was obtained which, on dehydrogenation with selenium, gave a hydrocarbon, $C_{15}H_{18}$, as shown by the analysis of the *picrate*, m. p. 102·5—104°, and the s.*-trinitrobenzene* derivative, m. p. 116—118°. If these reactions have proceeded normally, the hydrocarbon should be a naphthalene derivative with a methyl group in place of the hydroxymethylene group. The derivatives obtained were, however, not identical with the corresponding derivatives of 1 : 3-dimethyl-7-*iso*propylnaphthalene (see below), a fact which supports the conclusion that the carbon atom 3 (I) does not carry two hydrogen atoms. The picrate of the hydrocarbon $C_{15}H_{18}$ has the same melting point as the picrate of 1 : 4-dimethyl-7-*iso*propylnaphthalene (Ruzicka, Pieth, Reichstein, and Ehmann, *Helv. Chim. Acta*, 1933, **16**, 268). By the kindness of Professor L. Ruzicka we have been able to make a direct comparison and we find that the two picrates are not identical, a mixed melting point determination showing a depression of 15—20°. Moreover, the melting points of the *s*.-trinitrobenzene derivatives differ widely.

It appeared to us possible that the hydroxymethylene group might have been introduced on the methyl group attached to the carbon atom in the α-position to the carbonyl group. If this assumption were correct, the substance would be represented by (XVII) and should on reduction, followed by dehydrogenation, yield 1-ethyl-7-*iso*propylnaphthalene. Synthesis of this substance and a comparison of its crystalline derivatives with the derivatives of the hydrocarbon $C_{15}H_{18}$ obtained from hydroxymethylenecyperone showed this assumption to be incorrect. We are at present unable to assign a structure to this naphthalene hydrocarbon or to account for the formation of the hydroxymethylene derivative. If the hydrocarbon is a dimethyl*iso*propylnaphthalene, it can only be 1 : 8-dimethyl-7-*iso*propylnaphthalene, since the other isomeric hydrocarbons are known (see below). It is intended to synthesise this hydrocarbon. We know of no analogy for the formation of a hydroxymethylene derivative from a ketone in the absence of an adjacent $-CH_2$ group, although we may instance the abnormal behaviour of the αβ-unsaturated ketones, piperitone (Earl and Read, J., 1926, 2072) and ψ-codeionone (Lutz and Small, *J. Amer. Chem. Soc.*, 1935, **57**, 2652) with benzaldehyde.

Although α-cyperone can be readily purified by distillation, it is isomerised by prolonged digestion with oxalic or phthalic acid or by the action of alkali to yield an isomeric ketone, β-*cyperone*, from which a number of derivatives have been prepared. This ketone can only differ stereochemically from α-cyperone, since its *semicarbazone* yields on oxidation with ozone the same substance as α-cyperone semicarbazone. We would suggest that they differ in the spatial arrangement of the methyl group adjacent to the carbonyl group and that they are therefore related as menthone and *iso*menthone.

Prior to the experiments recorded in this paper Ruzicka and his collaborators (*loc. cit.*) synthesised 1 : 4- and 1 : 5-dimethyl-7-*iso*propylnaphthalene. We have now synthesised the 1 : 2- and the 1 : 6-isomeride and have prepared 1 : 3-dimethyl-7-*iso*propylnaphthalene by the dehydrogenation of the product obtained by the action of methylmagnesium iodide on tetrahydroeremophilone. For the synthesis of 1 : 2-dimethyl-7-*iso*propylnaphthalene, 2-methyl-7-*iso*propyl-1 : 2 : 3 : 4-tetral-1-one was prepared by the condensation of *homocuminyl bromide* with ethyl potassiomethylmalonate, followed by ring closure with sulphuric acid. Treatment of the resulting ketone with methylmagnesium iodide, followed by dehydrogenation with selenium, gave the required hydrocarbon. As the starting point for the synthesis of the 1 : 6-isomeride, *o*-tolylacetyl chloride was condensed with *iso*propylzinc iodide to give *o-methylbenzyl* iso*propyl ketone*, which was converted, by condensation with ethyl α-bromopropionate and replacement of the hydroxyl group by hydrogen by the usual series of reactions, into *ethyl γ-o-tolyl-α-methyl-β-*iso*propylbutyrate*. Ring closure of the ester with sulphuric acid gave 2 : 5-dimethyl-3-*iso*propyl-1 : 2 : 3 : 4-tetral-1-one, which, after reduction with sodium and alcohol, was dehydrogenated with selenium to the hydrocarbon.

In the following table we list the characteristic derivatives of these isomeric naphthalene hydrocarbons.

Hydrocarbon.	Picrate, m. p.	Styphnate, m. p.	*s*.-Trinitrobenzene, m. p.
1 : 2-Dimethyl-7-*iso*propyl	92—93·5°	—	108—110°
1 : 3- „	113—114·5	—	141—142
1 : 4- „	102·5—103	—	144·5—145·5 *
1 : 5- „	115·5—116·5	—	145—147 *
1 : 6- „	124—126	141—142°	—
1-Ethyl-7-*iso*propyl	65—67		79—81

* Ruzicka, Pieth, Reichstein, and Ehmann, *loc. cit.*

The derivatives of the synthetic 1 : 5-dimethyl-7-*iso*propylnaphthalene and the 1 : 3-dimethyl-7-*iso*propylnaphthalene from tetrahydroeremophilone have almost identical melting points. We have been able by the kindness of Professor Ruzicka to make a direct comparison of these derivatives. We find that, though there is no actual depression, the mixed melting points are decidedly less sharp than those of the pure individuals.

For the reasons already given (p. 670), we have synthesised also 1-ethyl-7-*iso*propylnaphthalene. This was prepared from 7-*iso*propyl-1 : 2 : 3 : 4-tetral-1-one (obtained by the condensation of homocuminyl bromide with ethyl potassiomalonate, followed by ring closure) by the action of ethylmagnesium iodide, followed by dehydrogenation with selenium.

EXPERIMENTAL.

The crude essential oil * (ketone content, 33—54%) was treated with semicarbazide acetate, a solid semicarbazone, corresponding to approximately 54% of the total ketone content, separating; this, crystallised from alcohol, gave pure *α-cyperone semicarbazone* (see below). After separation of the solid semicarbazone the non-ketonic constituents of the oil were removed by steam; a liquid semicarbazone remained which could not be purified. This semicarbazone was only partly hydrolysed by oxalic or phthalic acid; it gave, in addition to a further quantity of α-cyperone, a ketone, b. p. 145—146°/5 mm., $d_{30^\circ}^{30^\circ}$ 0·9879, $n_D^{30^\circ}$ 1·5138, $[\alpha]_D^{30^\circ} + 28{\cdot}5^\circ$, $[R_L]_D$ 66·3 (Found : C, 82·2; H, 9·8. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). No crystalline derivatives could be prepared from this ketone, so its homogeneity is doubtful.

α-Cyperone.—The ketone, prepared from the pure semicarbazone by hydrolysis with oxalic acid in acetone solution and purified by distillation in steam, was a colourless mobile oil, b. p. 177°/20 mm., $d_{25^\circ}^{25^\circ}$ 0·9946, $n_D^{25^\circ}$ 1·5283, $[\alpha]_{5461} + 138^\circ$, $[\alpha]_{5780} + 118{\cdot}6^\circ$, $[R_L]_D$ 67·53 (calc., 66·15) (Found : C, 82·0; H, 10·3. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). Oxidation with percamphoric acid proceeded very slowly; after 24 hours, 1·2 atoms of oxygen per molecule had been absorbed and after 8 days about 1·7. The *semicarbazone*, prepared from the recovered ketone, crystallised from methyl alcohol in serrated prisms, m. p. 216°; $[\alpha]_{5461} + 178^\circ$ in chloroform (*c*, 5·0) (Found : C, 69·9; H, 9·4; N, 15·4. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·1; N, 15·3%). The *oxime* separated from methyl alcohol in long prismatic needles, m. p. 150·5°; $[\alpha]_{5461} + 134^\circ$ in ethyl alcohol (*c*, 1·35) (Found : C, 77·2; H, 10·0; N, 6·2. $C_{15}H_{23}ON$ requires C, 77·3; H, 9·9; N, 6·0%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–ethyl acetate in soft red needles with a bronze reflex, m. p. 209—210° (Found : C, 63·6; H, 6·6. $C_{21}H_{26}O_4N_4$ requires C, 63·6; H, 6·6%). The *nitroguanylhydrazone* was deposited from alcohol in clusters of long needles, decomp. 203—204°; $[\alpha]_D + 196^\circ$ in chloroform (*c*, 2·5) (Found: N, 21·7. $C_{16}H_{25}O_2N_5$ requires N, 21·9%).

Hydroxymethylene-α-cyperone.—To a well-cooled solution of α-cyperone (3 g.) in ether (50 c.c.) containing finely divided sodium (0·35 g.) in suspension, amyl formate (1·8 g.) was added. After 12 hours, the greater part of the sodium having dissolved, ice was added, and the brown alkaline solution separated. After extraction with ether, the solution was acidified with acetic acid and the oil which separated was dissolved in ether. Evaporation of the dried ethereal extract left hydroxymethylene-α-cyperone as a viscid brown oil giving an intense reddish-violet colour with alcoholic ferric chloride. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–ethyl acetate in rosettes of thin, dark brown prisms, m. p. 159—160° (Found : C, 62·1; H, 5·9. $C_{22}H_{26}O_5N_4$ requires C, 62·0; H, 6·1%).

Reduction of α-Cyperone.—(i) *Catalytic.* The ketone (5·2 g.) in ethyl alcohol (50 c.c.) was shaken with hydrogen in the presence of palladium-norit (Pd, 10%), 1041 c.c. (1·95 mols.) of hydrogen being absorbed. The *tetrahydro-α-cyperone* had b. p. 151—152°/14 mm., $d_{25^\circ}^{25^\circ}$ 0·9597, $n_D^{25^\circ}$ 1·4871, $[\alpha]_{5461} + 14{\cdot}8^\circ$ (mic.),† $[\alpha]_{5780} + 12{\cdot}4^\circ$ (mic.), $[R_L]_D$ 66·42 (calc., 67·08) (Found : C, 81·2; H, 11·6. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%). The *semicarbazone* separated from methyl alcohol as a crystalline powder, decomp. 173—175° (Found : C, 69·3; H, 10·5. $C_{16}H_{29}ON_3$ requires C, 68·8; H, 10·4%). The *oxime* was deposited from alcohol in soft needles, m. p. 116—117·5° (Found : C, 75·4; H, 11·5. $C_{15}H_{27}ON$ requires C, 75·9; H, 11·4%). The 2 : 4-*dinitrophenylhydrazone* formed clusters of fine orange needles, m. p. 151—152° (Found : C, 62·7; H, 7·6. $C_{21}H_{30}O_4N_4$ requires C, 62·7; H, 7·5%). Hydroxymethylene tetrahydro-α-cyperone, prepared in the usual manner, was a mobile oil giving with alcoholic ferric chloride an

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* The percentage of α-cyperone present in the oil was highest in the oils having a high dextrorotatory power. Some specimens of the oil were lævorotatory and gave no α-cyperone semicarbazone although they contained as much as 35% of ketones. This point is being further investigated.

† Rotations were observed in a 1 dm. tube, except those followed by " (mic.)," for which a ½ dm. microtube was used.

intense purple-red colour. The 2 : 4-*dinitrophenylhydrazone* separated from alcohol–ethyl acetate in red needles with a coppery sheen, m. p. 182—183° (Found: C, 61·7; H, 6·8. $C_{21}H_{30}O_5N_4$ requires C, 61·4; H, 7·0%).

(ii) *With sodium and alcohol.* To a solution of α-cyperone (10 g.) in ethyl alcohol (400 c.c.), sodium (40 g.) was added as rapidly as possible, the reaction being completed by heating on the water-bath. After removal of the ethyl alcohol in steam, the sesquiterpene alcohol was extracted with ether, the ether dried and evaporated, and the residual oil distilled under diminished pressure; *dihydro-α-cyperol* was obtained as an extremely viscid oil, b. p. 167—168°/15 mm., $n_D^{25°}$ 1·5121, $[\alpha]_{5461}$ + 17·7° (in ethyl alcohol; *c*, 2·26) (Found: C, 80·7; H, 11·4. $C_{15}H_{26}O$ requires C, 81·1; H, 11·7%). The 3 : 5-*dinitrobenzoate*, prepared by treating the alcohol with 3 : 5-dinitrobenzoyl chloride in pyridine solution, crystallised from alcohol in soft silky needles, m. p. 157—158° (Found: C, 63·5; H, 6·6. $C_{22}H_{28}O_6N_2$ requires C, 63·5; H, 6·7%).

Dehydrogenation of Dihydro-α-cyperol.—The alcohol (7·5 g.) was heated with selenium first at 200° and later at 250° for 40 hours. From the product, eudalene was isolated and identified as the picrate, m. p. 91—92°, both alone and in admixture with an authentic specimen; the styphnate had m. p. 117—118°.

Oxidation of α-Cyperone.—(i) *With ozone.* The ketone (11 g.) in ethyl acetate (55 c.c.), cooled in ice, was ozonised, the issuing gases being led through water, which at the end of the experiment gave the dimedone test for formaldehyde. After evaporation of the solvent, the ozonide was decomposed with water and gave a keto-acid (7·3 g.). This was esterified with diazomethane; the liquid *ester*, b. p. 190—197°/11 mm., was not quite pure (Found: C, 64·3; H, 8·4. $C_{15}H_{24}O_5$ requires C, 63·4; H, 8·5%). The *semicarbazone*, which crystallised from alcohol, decomposed at 245—246° (Found: C, 56·8; H, 7·9. $C_{16}H_{27}O_5N_3$ requires C, 56·4; H, 7·9%).

The acid obtained by the hydrolysis of the ester was a yellow oil, which reduced Fehling's solution but gave no crystalline derivatives with carbonyl reagents. With sodium hypobromite its alkaline solution gave only a faint turbidity.

(ii) *With hydrogen peroxide.* To the ketone (2·4 g.) in methyl alcohol (25 c.c.), a mixture of 4*N*-sodium hydroxide (2·8 c.c.) and 15% hydrogen peroxide (5·5 c.c.) was added; considerable heat was generated. After 12 hours water was added, and the methyl alcohol removed in steam. The neutral oil (β-cyperone) was extracted with ether, and the alkaline solution acidified; a viscid oil separated. This was dissolved in ether, removal of the solvent yielding an oil, which partly crystallised. The acid was dissolved in aqueous ammonia, the gummy calcium salt precipitated by calcium chloride removed, the filtrate acidified, and the liquid acid extracted with ether. The oil remaining after removal of the solvent solidified and after draining on porous porcelain was recrystallised from either formic acid or methyl alcohol. The *acid* separated in fine needles, m. p. 112°; $[\alpha]_{5461}$ + 62·6° in methyl alcohol (*c*, 2·22) (Found: C, 69·1; H, 8·7. $C_{13}H_{20}O_3$ requires C, 69·6; H, 8·9%). It decolorised potassium permanganate in alkaline solution, but was not attacked by sodium hypobromite or by Fuson's reagent. The *semicarbazone* crystallised from methyl alcohol in long prisms, decomp. 180—181° (Found: C, 59·9; H, 8·2. $C_{14}H_{23}O_3N_3$ requires C, 59·8; H, 8·2%). The *phenylsemicarbazone* separated from ethyl alcohol in well-formed prisms, decomp. 200° (Found: C, 67·1; H, 7·6. $C_{20}H_{27}O_3N_3$ requires C, 67·2; H, 7·6%).

Oxidation of α-Cyperone Semicarbazone with Ozone.—The semicarbazone (2 g.) was suspended in acetic acid (40 c.c.), and ozone passed through at room temperature until all the solid had dissolved. The solvent was removed under diminished pressure, and the residual oil stirred with a little methyl alcohol; the crystalline solid obtained, recrystallised from alcohol, separated in well-formed needles, decomp. 185—187° (Found: C, 58·2; H, 7·4. $C_{15}H_{23}O_4N_3$ requires C, 58·3; H, 7·4%). The *semicarbazone* gave no colour with ferric chloride; it reduced Fehling's solution and ammoniacal silver nitrate. Its alcoholic solution gave with semicarbazide acetate an amorphous powder which was very sparingly soluble in all the ordinary solvents and could not be recrystallised (Found: C, 41·9, 42·1; H, 6·8, 6·6; N, 31·0%).

Oxidation of Dihydro-α-cyperol with Ozone.—The alcohol (5·1 g.) in ethyl acetate (20 c.c.), cooled in ice, was oxidised with ozone. Formaldehyde was identified in the issuing gases by preparation of the dimedone derivative. After evaporation of the solvent, the ozonide was decomposed by boiling water and separated into acid and neutral portions. No crystalline derivatives of the acid fraction could be prepared and this was not further examined. The neutral oil (3·1 g.), b. p. 200—205°/17 mm., was oxidised to the corresponding diketone by chromic acid in acetic acid solution. This was a viscid oil, which gave no bromoform with sodium hypobromite in alkaline solution and did not react with Fuson's reagent. The *dioxime* crystallised from butyl alcohol in small hexagonal plates, decomp. 258—259°, sintering at 247° (Found: C, 67·0; H, 9·7. $C_{14}H_{24}O_2N_2$ requires C, 66·7; H, 9·5%). The *disemicarbazone* separated from the same solvent as a microcrystalline powder, decomp. 251—252° (Found: C, 56·8; H, 8·3. $C_{16}H_{28}O_2N_6$ requires C, 57·1; H, 8·3%).

In a preliminary experiment in which an impure specimen of the alcohol, containing some α-cyperol, was used, the neutral ozonolysis product gave a *di-* or *tri-phenylsemicarbazone*, decomp. 222—223°, which crystallised from butyl alcohol (Found: C, 64·5, 64·7; H, 6·7, 6·5. $C_{28}H_{36}O_4N_6$ requires C, 64·6; H, 6·9. $C_{35}H_{43}O_4N_9$ requires C, 64·4; H, 6·6%). The constitution of this substance is referred to on p. 669.

Oxidation of Dihydro-α-cyperyl 3 : 5-*Dinitrobenzoate*.—Ozone was passed through a solution of the benzoate (2·5 g.) in ethyl acetate (25 c.c.) until it was present in excess. The issuing gases contained a considerable quantity of formaldehyde, identified as the dimedone derivative (0·2 g.). After removal of the ethyl acetate the ozonide was decomposed by boiling water, the small amount of acid present was neutralised with potassium bicarbonate, and the oil which had separated was extracted with ether. Evaporation of the dried extract gave a gum (2·2 g.), which, except for a small quantity of resinous impurity, crystallised from acetic acid (70%) in fine needles, decomp. 143° with previous sintering. After two further recrystallisations from the same solvent and two from alcohol, the *ketone* was obtained in soft needles, m. p. 148—149°, not depressed by dihydro-α-cyperyl 3 : 5-dinitrobenzoate (Found: C, 60·2; H, 6·1. $C_{21}H_{26}O_7N_2$ requires C, 60·3; H, 6·2%). The ketone reacted readily with the ordinary carbonyl reagents, but crystalline derivatives could not be prepared. With Fuson's reagent, iodoform, m. p. 119—120°, was formed; the alkaline solution on acidification deposited a gummy acid, from which a small quantity of 3 : 5-dinitrobenzoic acid was separated, but the main product of the oxidation could not be crystallised.

Conversion of Tetrahydro-α-cyperone into 1 : 2-*Dimethyl*-7-iso*propylnaphthalene*.—The ketone (9·7 g.) was treated with the Grignard reagent prepared from magnesium (1·15 g.) and methyl iodide (6·8 g.). As the product still contained a trace of ketone, it was treated with a further quantity of the reagent. The final product, a mixture of unsaturated hydrocarbon and alcohol, b. p. 137—150°/11 mm., was dehydrogenated by heating with selenium first at about 200° and finally at 300° for 40 hours. The product, b. p. 140—150°/12 mm., gave a *picrate* crystallising from alcohol in feathery orange-yellow needles, m. p. 92—93° (Found: C, 58·9; H, 4·8. $C_{21}H_{21}O_7N_3$ requires C, 59·0; H, 4·9%), and a s.-*trinitrobenzene* derivative separating from alcohol in yellow needles, m. p. 107—109° (Found: C, 60·9; H, 4·9. $C_{21}H_{21}O_6N_3$ requires C, 61·3; H, 5·1%). These derivatives were identical in all respects with the corresponding derivatives of 1 : 2-dimethyl-7-*iso*propylnaphthalene the synthesis of which is described on p. 674.

Reduction and Dehydrogenation of Hydroxymethylene-α-cyperone.—Reduction of hydroxymethylene-α-cyperone (10 g.) by hydrogen in the presence of palladium-norit under 3 atm. pressure was very slow and after 70 hours only about half the calculated quantity of hydrogen had been absorbed. The reduction was therefore completed with sodium and alcohol, and the very viscid oil obtained (5 g.) dehydrogenated by heating with selenium at 300—320° for 23 hours. The product, b. p. 140—160°/10 mm., yielded a *picrate*, which crystallised from methyl alcohol in short orange needles, m. p. 102·5—104° (Found: C, 59·2; H, 5·3. $C_{21}H_{21}O_7N_3$ requires C, 59·0; H, 4·9%), and a s.-*trinitrobenzene* derivative crystallising from alcohol in bright yellow needles, m. p. 116—118° (Found: C, 61·4; H, 5·2. $C_{21}H_{21}O_6N_3$ requires C, 61·3; H, 5·1%).

α-Cyperene.*—α-Cyperone semicarbazone (2 g.) was heated with sodium ethoxide (ethyl alcohol, 3 c.c.; sodium, 0·25 g.) at 200° for 6—7 hours. The product from several such experiments was isolated by steam distillation and purified by distillation over sodium, the *hydrocarbon*, b. p. 132—133°/15 mm., obtained being not quite pure (Found: C, 87·2; H, 11·5. $C_{15}H_{24}$ requires C, 88·2; H, 11·8%). Oxidation with ozone in ethyl acetate solution at 0° gave formaldehyde (dimedone test), but no acetone was formed on decomposition of the ozonide with hot water. The main product of the oxidation was a neutral substance, which gave amorphous derivatives with the usual carbonyl reagents. It reduced ammoniacal silver nitrate solution and gave a positive iodoform test with Fuson's reagent, but no colour with ferric chloride. A small quantity of an acid was obtained also. This gave no crystalline derivatives with carbonyl group reagents, gave a positive Fuson test, but did not reduce ammoniacal silver nitrate solution and gave no colour with ferric chloride.

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* The name cyperene has been given to a sesquiterpene of unknown constitution obtained by Kimura and Ohtani (*J. Pharm. Soc. Japan*, 1928, **48**, 128) from the rhizomes of *Cyperus rotundus*.

The hydrocarbon, b. p. 130—132°/14 mm., was recovered unchanged after treatment with sodium and ethyl or amyl alcohol and on titration with percamphoric acid it then showed an absorption of oxygen corresponding to 1·9 ethylenic linkages.

β-*Cyperone.*—As mentioned on p. 670, α-cyperone was isomerised when digested with an aqueous solution of oxalic acid for some hours, a change which was also effected by the action of methyl-alcoholic potassium hydroxide solution. The new ketone was converted into the *semicarbazone*, which crystallised from methyl alcohol in prisms, decomp. 207° (Found: C, 69·9; H, 9·0; N, 15·0. $C_{16}H_{25}ON_3$ requires C, 69·8; H, 9·1; N, 15·3%). The semicarbazone was phototropic, becoming yellow on exposure to light, the colourless form being obtained after recrystallisation from methyl alcohol. β-*Cyperone*, regenerated from the semicarbazone by digestion with oxalic acid in acetone solution, was a colourless mobile oil, b. p. 175—176°/16 mm., $d_{25^\circ}^{25^\circ}$ 0·9945, $n_D^{20^\circ}$ 1·5414, $[\alpha]_{5461}$ + 239° (Found: C, 82·2; H, 10·3. $C_{15}H_{22}O$ requires C, 82·6; H, 10·1%). The *oxime* crystallised from methyl alcohol in prismatic needles, m. p. 138°, $[\alpha]_{5461}$ + 217° in alcohol (*c*, 1·45) (Found: C, 76·9; H, 9·5; N, 5·8. $C_{15}H_{23}ON$ requires C, 77·3; H, 9·9; N, 6·0%). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol–ethyl acetate in red needles with a metallic reflex, decomp. 218—219° (Found: C, 63·2; H, 6·5. $C_{21}H_{26}O_4N_4$ requires C, 63·6; H, 6·6%). The *nitroguanylhydrazone* crystallised from alcohol in needles, m. p. 197°; $[\alpha]_D$ + 220° in chloroform (*c*, 2·5) (Found: N, 21·6. $C_{16}H_{25}O_2N_5$ requires N, 21·9%). Ozonolysis of β-cyperone semicarbazone gave a semicarbazone, m. p. 185—187°, identical with that obtained by the ozonolysis of α-cyperone semicarbazone (compare p. 672) (Found: C, 58·0; H, 7·3%).

Synthesis of 1 : 2-*Dimethyl*-7-iso*propylnaphthalene.*—*Homocuminyl alcohol.* Homocumic acid was prepared quantitatively from the corresponding mandelic acid by reduction with tin and hydrochloric acid. The use of amalgamated zinc in place of tin gave inferior results.

Ethyl homocuminate (41·5 g.) in alcohol (300 c.c.) was added in one portion to sodium (29 g.). When the reaction had moderated, the mixture was maintained at 130° until all the sodium had dissolved. The ethyl alcohol was removed in a current of steam, and the cooled solution extracted with ether. After drying and removal of the solvent, *homocuminyl alcohol* (20·3 g.), b. p. 129°/10 mm., was obtained (Found: C, 80·4; H, 9·8. $C_{11}H_{16}O$ requires C, 80·4; H, 9·8%). The p-*xenylcarbamate* crystallised from benzene–ligroin in fine needles, m. p. 144—145° (Found: C, 80·4; H, 7·0. $C_{24}H_{25}O_2N$ requires C, 80·2; H, 7·0%).

Homocuminyl bromide. Homocuminyl alcohol (34 g.) was added to phosphorus tribromide (28 g.), and the mixture heated on the water-bath for 2 hours. The product was decanted from the phosphorous acid into ice-water and recovered with ether. *Homocuminyl bromide* (42 g.), b. p. 136°/14 mm., was a pleasant-smelling mobile oil (Found: Br, 35·4. $C_{11}H_{15}Br$ requires Br, 35·3%).

Ethyl homocuminylmethylmalonate. To a suspension of ethyl methylpotassiomalonate (from ethyl methylmalonate, 24 g., and potassium, 5·3 g.) in benzene (50 c.c.), homocuminyl bromide (30 g.) was added, and the mixture heated on the water-bath for 100 hours. Isolated in the usual manner, *ethyl homocuminylmethylmalonate* (34 g.) was obtained as a somewhat viscid oil, b. p. 200°/13 mm. (Found: C, 71·0; H, 8·5. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·7%).

2-*Methyl*-7-iso*propyl*-1 : 2 : 3 : 4-*tetral*-1-*one.* The ester (38 g.) was heated on the water-bath with sulphuric acid (160 c.c.) and water (60 c.c.) for 3 hours. After dilution with water the ketone was extracted with ether, the solvent removed, and some unchanged ester hydrolysed by digestion with methyl-alcoholic potassium hydroxide solution. The ketone (10 g.), separated by the addition of water and extraction with ether, was a mobile colourless oil, b. p. 155—160°/12 mm. The *phenylsemicarbazone* crystallised from alcohol in prisms, m. p. 180—181° (Found: C, 75·4; H, 7·6. $C_{21}H_{25}ON_3$ requires C, 75·2; H, 7·5%). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol–ethyl acetate in deep red prisms, frequently twinned, m. p. 177—178° (Found: N, 14·6. $C_{20}H_{22}O_4N_4$ requires N, 14·7%).

The above ketone (10 g.) was added to the Grignard reagent prepared from methyl iodide (15 g.) and magnesium (2·4 g.). After 24 hours, the solution was heated on the water-bath for 1 hour, and the product isolated in the usual manner. The oil (8 g.), b. p. 135—140/10 mm., consisted mainly of hydrocarbon and was dehydrogenated by heating with selenium (15 g.) at 300° for 28 hours, yielding 1 : 2-dimethyl-7-*iso*propylnaphthalene as a colourless oil, b. p. 149—151°/9 mm. The *picrate* crystallised from alcohol in orange-yellow needles, m. p. 92—93·5° (Found: N, 9·7. $C_{21}H_{21}O_7N_3$ requires N, 9·8%), and the s.-*trinitrobenzene* derivative from alcohol in yellow needles, m. p. 108—110° (Found: N, 9·8. $C_{21}H_{21}O_6N_3$ requires N, 10·2%).

1 : 3-*Dimethyl*-7-iso*propylnaphthalene.*—Tetrahydroeremophilone (11 g.) was added to the

Grignard reagent prepared from methyl iodide (17·7 g.) and magnesium (3 g.) and after 20 hours the solution was heated on the water-bath for 1 hour. The product (10·4 g.), isolated in the usual manner, had b. p. 145—150°/7 mm. It was dehydrogenated by heating with selenium at 300—310° for 24 hours. The hydrocarbon obtained gave a *picrate*, which crystallised from alcohol in silky orange-yellow needles, m. p. 113—114·5° (Found : C, 59·2; H, 4·8. $C_{21}H_{21}O_7N_3$ requires C, 59·0; H, 4·9%). The s.-*trinitrobenzene* derivative formed bright yellow needles, m. p. 141—142° (Found : C, 61·1; H, 5·0. $C_{21}H_{21}O_6N_3$ requires C, 61·3; H, 5·1%).

Synthesis of 1 : 6-*Dimethyl*-7-iso*propylnaphthalene*.—o-*Methylbenzyl* iso*propyl ketone*. *o*-Tolylacetic acid was prepared from ω-bromo-*o*-xylene *via* the nitrile. A better return of the monobromo-compound on the *o*-xylene used was obtained by using less bromine than that given by Atkinson and Thorpe (J., 1907, **91**, 1695). *o*-Xylene (75 g.) on treatment with bromine (90 g.) at 130° gave ω-bromide (77·3 g.), b. p. 110—114°/16 mm., and *o*-xylene (23 g.). *o*-Tolylacetyl chloride, prepared by the action of thionyl chloride on the acid, had b. p. 111—112°/16 mm.

A mixture of *iso*propyl iodide (60 g.), ethyl acetate (10 c.c.), and ligroin (b. p. 105—115°) (21 c.c.) was cautiously heated with a zinc–copper couple (50 g.) until the reaction began; the temperature was then gradually raised to 110° and maintained for 30 minutes. The solution of *iso*propylzinc iodide thus prepared was mixed with toluene (21 c.c.), decanted from the excess of the zinc–copper couple, and well cooled in ice in a vessel from which moisture was excluded. A mixture of *o*-tolylacetyl chloride (26·5 g.) and toluene (25 c.c.) was slowly added (mechanical stirring) and after addition was complete the solution was allowed to come slowly to room temperature, again cooled, and water added; the slight precipitate of zinc hydroxide was dissolved with dilute sulphuric acid. The product was extracted with ether, the extract washed three times with aqueous ammonia, then with water, dilute sulphuric acid and water, dried, and the ether removed. The residue was refluxed with alcoholic potassium hydroxide (KOH, 10 g.) to hydrolyse the ester formed as a by-product, and steam-distilled, and the oil which passed over was collected in ether. The hydrocarbon solvent was removed at 100 mm., and the residue distilled at 13 mm., o-*methylbenzyl* iso*propyl ketone*, b. p. 125—126°, $d_{25^\circ}^{25^\circ}$ 0·9652, $n_D^{25^\circ}$ 1·5070, being obtained as a slightly greenish oil which became colourless on standing over-night (yield, 40%) (Found : C, 81·7; H, 9·1. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). The *semicarbazone* crystallised from methyl alcohol in prisms, m. p. 128—129° (Found : C, 66·9; H, 8·3. $C_{13}H_{19}ON_3$ requires C, 66·9; H, 8·2%); the *phenylsemicarbazone* separated from alcohol in prismatic needles, m. p. 183° (Found : C, 73·7; H, 7·4. $C_{19}H_{23}ON_3$ requires C, 73·8; H, 7·4%).

Ethyl γ-o-*tolyl*-α-*methyl*-β-iso*propylbutyrate*. The ketone (28 g.) and ethyl α-bromopropionate (39 g.) were added to zinc (18·5 g.) covered with dry ether and the mixture was heated on the water-bath, the reaction being initiated by the addition of methylmagnesium iodide. After 6 hours the product was treated with ice and dilute hydrochloric acid, and the ether separated, washed with dilute sulphuric acid, potassium bicarbonate solution, dried, and evaporated. The residue, b. p. 165—195°/16 mm., was dehydrated by heating with potassium hydrogen sulphate (40 g.) for 2 hours at 195—200°. The product, without further purification, was reduced with hydrogen under 3 atms. in the presence of palladium-norit catalyst in alcoholic solution. After removal of the alcohol *ethyl* γ-o-*tolyl*-α-*methyl*-β-iso*propylbutyrate* distilled at 165°/13 mm. (Found : C, 78·0; H, 9·7. $C_{17}H_{26}O_2$ requires C, 77·9; H, 9·9%).

2 : 5-*Dimethyl*-3-iso*propyl*-1 : 2 : 3 : 4-*tetral*-1-*one*. The above-mentioned ester (24 g.) was heated on the water-bath with sulphuric acid (acid, 122·5 c.c.; water, 52·5 c.c.) for 1 hour, and the mixture poured into water. The oil was extracted with ether, the solvent removed, and the residue refluxed with an excess of alcoholic potassium hydroxide solution for 30 minutes. After addition of water, the ketone was again collected in ether, the solution dried, and the solvent removed; the ketone then had b. p. 185—190°/22 mm. The *phenylsemicarbazone* crystallised from alcohol in prismatic needles, m. p. 222—223° (Found : C, 75·2; H, 7·8. $C_{22}H_{27}ON_3$ requires C, 75·6; H, 7·7%).

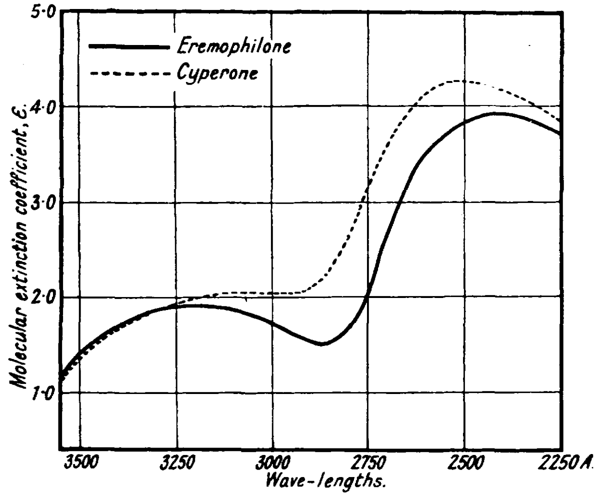
The ketone (11 g.) in boiling ethyl alcohol (200 c.c.) was treated with sodium (20 g.); after reduction was complete, the ethyl alcohol was removed in steam, and the product extracted with ether. Without further purification the tetralol was dehydrogenated by heating with selenium at 280° for 15 hours. The 1 : 6-dimethyl-7-*iso*propylnaphthalene, after purification through the picrate, had b. p. 154—158°/13 mm. The *picrate* crystallised from ethyl alcohol in orange-red needles, m. p. 124—126° (Found : C, 59·6; H, 5·0. $C_{21}H_{21}O_7N_3$ requires C, 59·0; H, 4·9%). The *styphnate* was deposited from ethyl alcohol in silky orange-yellow needles, m. p. 141—142° (Found : C, 57·0; H, 4·8. $C_{21}H_{21}O_8N_3$ requires C, 56·9; H, 4·7%).

Synthesis of 1-*Ethyl*-7-iso*propylnaphthalene*.—*Ethyl homocuminylmalonate* was prepared from homocuminyl bromide under conditions similar to those used for the preparation of ethyl homocuminylmethylmalonate (p. 674), ethyl methylmalonate being replaced by ethyl malonate. The ester (20 g. from the bromide, 20 g.) had b. p. 198°/13 mm. (Found : C, 70·4; H, 8·5. $C_{18}H_{26}O_4$ requires C, 70·6; H, 8·5%). It was converted into 7-*iso*propyl-1 : 2 : 3 : 4-tetral-1-one, b. p. 158—160°/17 mm., with sulphuric acid under conditions similar to those described above. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethyl acetate in soft needles, m. p. 223—224° (Found : C, 62·1; H, 5·5. $C_{19}H_{20}O_4N_4$ requires C, 62·0; H, 5·4%).

The tetralone (6 g.) was treated with a Grignard reagent prepared from magnesium (2 g.) and ethyl iodide (12·5 g.), and the product, recovered in the usual manner, dehydrogenated by heating with selenium at 300—320° for 40 hours. From the crude 1-ethyl-7-*iso*propylnaphthalene, b. p. 135—145°/9 mm., a *picrate* was prepared in methyl-alcoholic solution, which crystallised from the same solvent, in which it was somewhat readily soluble, in deep yellow needles, m. p. 65—67°, although the melt did not become clear until the temperature was 20—30° higher. This m. p. was unchanged after several crystallisations, and further fractionation of the material in the mother-liquors failed to yield any indication of the presence of a second substance (Found : C, 59·0; H, 5·1. $C_{21}H_{21}O_7N_3$ requires C, 59·0; H, 4·9%). The s.-*trinitrobenzene* derivative crystallised from ethyl alcohol in yellow needles, m. p. 79—81° (Found : C, 61·7; H, 5·3. $C_{21}H_{21}O_6N_3$ requires C, 61·2; H, 5·1%).

The Absorption Spectrum of α-Cyperone and its Indications as to the Probable Structure of the Compound (By A. E. Gillam).

Before α-cyperone had been successfully reduced to a product of known constitution it was suggested that the nature of the absorption spectrum might throw some light on its molecular structure. In particular it was important to know whether the C:O and the C:C linkages known to be present were conjugated or not.



The absorption spectrum was determined on a Hilger E_3 quartz spectrograph fitted with a Spekker photometer. The absorption curve (see fig.) will be seen to be made up of two bands : the one of low intensity and negligible persistence at 3000—3200 A. is due to a C:O group, and the short-wave band of high intensity is typical of a conjugated system of double bonds.

It was known that the compound was an unsaturated ketone, and if the C:O and C:C bonds were widely separated in the molecule one would expect only the absorption characteristic of the C:O group to be exhibited. Thus methylheptenone, $CHMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3$, has $\lambda_{max.}$ at 2780 A. and log $\varepsilon_{max.}$ = 1·72, data closely comparable with those of acetone ($\lambda_{max.}$ 2750 A., log $\varepsilon_{max.}$ = 1·23).

The results show that the absorption spectrum of α-cyperone is quite different from that of either acetone or methylheptenone, being in fact very similar to that of mesityl oxide (Morton, J., 1926, 719), a very simple αβ-unsaturated ketone. Various typical saturated and unsaturated ketones have also been examined by Menschik, Page, and Bossert (*Annalen*, 1933, **495**, 225), who have demonstrated clearly that absorption of the type shown by mesityl oxide can be taken to indicate the presence of a C:O group conjugated with a C:C group. The evidence of absorption spectra thus strongly supports the view that α-cyperone is an αβ-unsaturated ketone. In order to substantiate this further, the absorption spectrum of another compound closely analogous to α-cyperone, *viz.*, eremophilone, and definitely known to be an αβ-unsaturated ketone was examined and found to be closely similar to that of α-cyperone (see fig.). The following table shows some relevant numerical data for compounds with the chromophoric group C:C—C:O.

	" Ethylene " band.		" Ketone " band.		Literature.
	$\lambda_{max.}$, A.	Log ε.	$\lambda_{max.}$, A.	Log ε.	
Cholestenone	2430	4·30	3120	2·07	Heilbron, Morton, and Sexton, J., 1928, 719.
Mesityl oxide	2350	4·14	3130	1·74	Morton, *loc. cit.*
Eremophilone......	2430	3·90	3190	1·89	This paper.
α-Cyperone	2510	4·28	3120	2·07	,,

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