

The Structure of Cyperone. Part III. Natural and Synthetic
Cyperones.*

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The synthesis of α - and β -cyperone (Adamson, McQuillin, Robinson, and Simonsen, *J.*, 1937, 1576) has been improved so as to lead to the intermediate crystalline ketol (III) in good yield. The configuration of this ketol has been established, as well as those of the optically pure ketones (IV) and (V). Natural α -cyperone is shown to be the 6-epimer of the synthetic (IV). Observations are made on the course of the synthesis and on the mode of racemisation of ketones of type (IV).

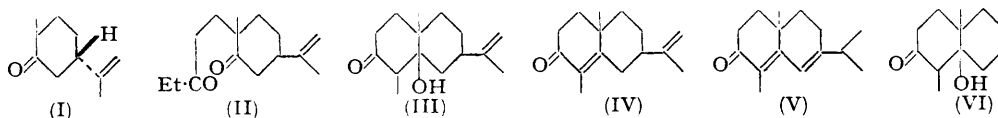
ADAMSON, McQUILLIN, ROBINSON, and SIMONSEN (*loc. cit.*) prepared synthetic α - and β -cyperones which showed a general correspondence in their properties and in those of their derivatives with natural α -cyperone and the ketone obtained from it by isomerisation. There were, however, differences, ascribed to partial racemisation of the synthetic material. These differences, the later recognition of the "natural" β -cyperone as a mixture (McQuillin, *J.*, 1951, 716), and the uncertainty as to the homogeneity of α -cyperone (cf. Part II *) led us to re-examine this synthesis.

Adamson *et al.* (*loc. cit.*) condensed (–)-dihydrocarvone (I) with diethylmethyl-3-oxopentylammonium iodide in ether-pyridine to obtain a first condensation product consisting largely of a crystalline material, $C_{15}H_{24}O_2$, at that time regarded as the diketone (II). On the basis of a strong hydroxyl absorption at 3510 cm.^{-1} and a typical saturated ketone-carbonyl frequency at 1695 cm.^{-1} this substance must now be given the ketol

* Part II, preceding paper.

structure (III). The conditions for the condensation have been altered so as to afford this crystalline ketol in greatly improved yield and as the main product. An analogous crystalline ketol (VI) has been isolated from a similar condensation with 2-methylcyclohexanone; Gunstone and Heggie (*J.*, 1952, 1437) failed to observe this. Before discussing the reaction, however, it will be convenient to consider the configuration of the products.

The ketol (III), $[\alpha]_{5461} -54^\circ$, was smoothly dehydrated in *N*-aqueous-alcoholic hydrochloric acid at room temperature, or by refluxing in *N*-alcoholic potassium hydroxide, to give the same unsaturated ketone (IV), $[\alpha]_{5461} +210^\circ$, $+217^\circ$ (oxime, $[\alpha]_{5461} +233^\circ$; semicarbazone, $[\alpha]_{5461} +244^\circ$). From the correspondence in rotation of the ketones and derivatives these preparations are evidently optically pure.



The ketol (III) was not dehydrated by absorption on alumina, or by many hours' refluxing with pyridine and piperidine in benzene or alcohol (cf. Friedman and Robinson, *Chem. and Ind.*, 1951, 777). By treatment with 50% v/v sulphuric acid at room temperature the ketol was dehydrated with concomitant isomerisation to the fully conjugated ketone (V), $[\alpha]_{5461} +678^\circ$ (oxime, $[\alpha]_{5461} +307^\circ$; semicarbazone, $[\alpha]_{5461} +401^\circ$), which is regarded as optically pure. Similar acid treatment of the ketone (IV) led to a ketone (V), $[\alpha]_{5461} +639^\circ$. The ketone (V) of $[\alpha]_{5461} +678^\circ$ was not racemised by this treatment and the reason for this difference is discussed below.

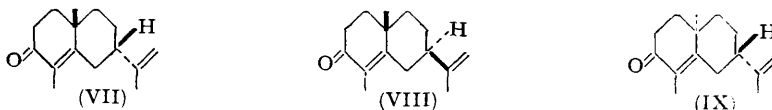
The ketone (IV) on hydrogenation in alcohol gave a tetrahydro-ketone consisting largely of a single crystalline isomer, $[\alpha]_{5461} +25.8^\circ$, and with lithium in liquid ammonia (Sondheimer, Mancera, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1953, 75, 1282; Barton, Ives, and Thomas, *J.*, 1954, 903) gave a crystalline dihydro-ketone, $[\alpha]_{5461} +25.9^\circ$, as sole product and in high yield. Reduction of conjugated steroid-enones by the latter method leads to the stable (*trans*-)bridge-head configuration, and in the present instance this reduction must lead also to the more stable α (equatorial)-configuration for the 4-methyl group. Inspection of the models shows considerable steric interaction in the 4 β -methyl configuration with *trans*-ring fusion.

Klyne (*J.*, 1953, 3079) has already indicated that the asymmetry of β -cyperone must be configurationally the same as at the corresponding centre in the steroid molecule. Revised molecular-rotation values based on the optically pure ketones now available are listed in

TABLE I.

	$[M]_{5461}$	Δ		$[M]_D$	Δ
Dihydrocyperone, synth. ...	+57°	+416°	Cholestan-3-one	+158°	+184°
Synthetic ketone (IV)	+473	+1395	Cholest-4-en-3-one	+342	-1328
Synthetic ketone (V)	+1452		Cholesta-3 : 5-dien-7-one ...	-1170	

Table 1. The configuration of the sterols and terpenes having been correlated (Prelog, *Helv. Chim. Acta*, 1953, 36, 308 *et seq.*; Mills, *Chem. and Ind.*, 1953, 218; Cornforth, Yenhotzky, and Popjak, *Nature*, 1954, 173, 536; Arigoni, Riniker, and Jeger, *Helv. Chim. Acta*, 1954, 37, 878) and the configuration of (—)-dihydrocarvone being known (cf. Hüchel,



J. prakt. Chem., 1941, 157, 225; McNiven and Read, *J.*, 1952, 159; Birch, *Ann. Reports*, 1950, 47, 191), synthetic cyperone may be given the absolute configuration (VII). This synthetic ketone and its derivatives, the natural cyperone, and the earlier synthetic material of Adamson *et al.* (*loc. cit.*) are compared in Table 2. In the absence of any large proportion of the *isopropylidene* isomer (cf. preceding paper) the differences in physical properties

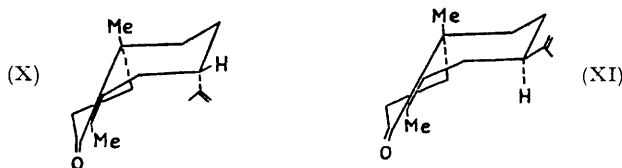
indicated point unmistakably to natural cyperone's being the 6-epimer of the synthetic ketone, *i.e.*, (VIII). The corresponding conformations (X = synthetic and XI = natural) show clearly that the latter represents the more completely "trans"-arrangement. The earlier synthetic material (Adamson *et al.*, *loc. cit.*) was correctly described as partly racemic.

TABLE 2.

	Natural ¹	Synthetic	
		(a)	(b)
Ketones, $[\alpha]_{5461}$	+119.2°	+216.8°	+58.2° (68°) ²
n_D^{20}	1.5292	1.5343	1.5299
d	0.9946	1.006	1.012
Oximes, m. p.	150.5°	90°	144°
$[\alpha]_{5461}$	+134	+233	—
Semicarbazones, m. p.	216	177	202
$[\alpha]_{5461}$	+178	+244	+ 91.5
2 : 4-Dinitrophenylhydrazones, m. p.	210	202	—
Tetrahydro-ketone, $[\alpha]_{5461}$	+14.8	+25.9	—

¹ Cf. Bradfield, Hegde, Rao, Simonsen, and Gillam (*J.*, 1936, 667), and preceding paper. (a) Data from this work and (b) from Adamson *et al.* (*loc. cit.*). ² Redetermined in chloroform and, in parentheses, without solvent.

This assignment of the configuration (VIII) to natural cyperone is confirmed unequivocally by other evidence. The crystalline ketol (III) which forms the major product of condensation of (–)-dihydrocarvone and diethylmethyl-3-oxopentylammonium iodide was accompanied by a non-crystalline product, which on chromatography gave a dehydro-ketone corresponding with (IV), but optically impure, $[\alpha]_{5461}$ +42.4°, and affording two oximes, one dextro- and one *lævo*-rotatory. The latter oxime is clearly derived from the 9-epimer of (VII), *i.e.*, (IX), the enantiomorph of natural cyperone. It



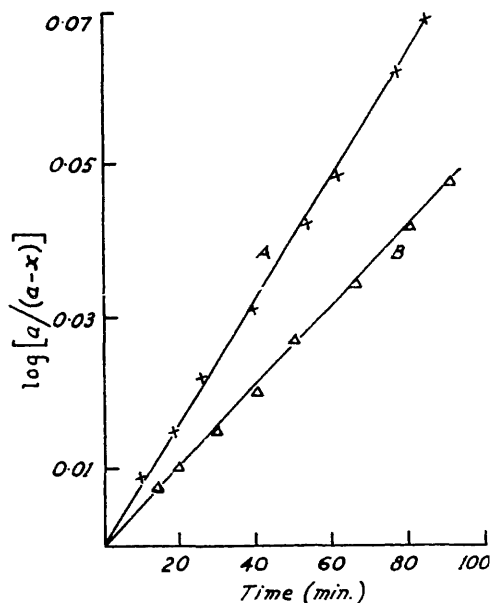
was this oxime which Dr. Crowfoot-Hodgkin (*cf.* Adamson *et al.*, *loc. cit.*) found crystallographically identical with the (dextrorotatory) oxime of natural cyperone. The "identity" is understandable only if the oximes are enantiomorphs, and it provides the strongest support for the configuration assigned to natural cyperone.

Taken together with the work of Adamson *et al.* (*loc. cit.*) these results throw light also on the course of the metho-salt-sodio-ketone condensation which is the basis of these syntheses. (i) When condensation is carried out in ether (du Feu, McQuillin, and Robinson, *J.*, 1937, 53) with or without a small addition of pyridine (Adamson *et al.*, *loc. cit.*) the metho-salt is insoluble and the reaction is heterogeneous and slow: the yield of condensation product is 30%, including 15–20% of the crystalline ketol (III). (ii) By using sufficient pyridine to ensure rapid reaction in homogeneous medium the total yield is 70%, of which 60% is the ketol (III) in the condensation with (–)-dihydrocarvone; but from 2-methylcyclohexanone the ketol (VI) was isolated in only small amount. (iii) Whilst mild conditions of dehydration of the cyperone ketol (III) lead, as already noted, to an optically pure dehydro-ketone (VII) the use by Adamson *et al.* (*loc. cit.*) of strong base (dry sodium ethoxide in ether) led to the mixture of (VII) and (IX) by more or less complete inversion at C₉. From this last observation it is clear that the reaction is, as might be expected, reversible. Its course may be represented as in (A) or possibly through a cyclic transition state (B). The importance of ensuring rapid reaction (and neutralisation) during the condensation is then apparent; not only is the product formed in the initial, kinetically controlled step otherwise inverted to a thermodynamically more stable mixture, but the process is accompanied by loss of yield through self-condensation of the vinyl ketone addend released.

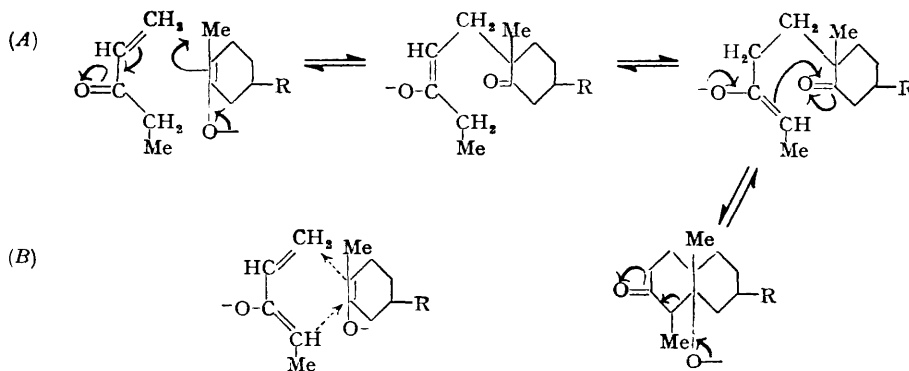
It was noted under (ii) that the 2-methylcyclohexanone ketol (VI) formed only a minor part of the reaction product, *i.e.*, the ketol is in this case more readily dehydrated. By following the formation of unsaturated ketone from the absorption at 250 μ it was found, however, that in *N*-aqueous-alcoholic hydrochloric acid the reverse is the case; the cyperone ketol (III) is the more easily dehydrated (*cf.* Figure). The isopropenyl

Rate of dehydration of ketols in *N*-aqueous-alcoholic hydrochloric acid:

A, the cyperone ketol (III);
B, the ketol (VI).



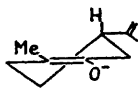
substituent in (III) would be expected to influence dehydration in two ways, (*a*) by facilitating the transition state through increased intramolecular compression, (*b*) by steric retardation of removal of the hydrogen atom or hydroxyl group concerned in the initiating step. The effect of the increased compression should, however, be independent of the initiating step, and we therefore infer that the hydrogen atom and the hydroxyl group in



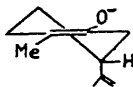
the cyperone ketol are respectively *syn* and *anti* with respect to the side chain, leading to the provisional (*cis*-)configuration (XIV) for this substance.

The side-chain substituent also evidently leads to a high measure of stereospecificity in the initial condensation. The sodio-enolate ion of (–)-dihydrocarvone may take up the conformations (XII) and (XIII) of which the former will be the more stable (*cf.* Barton, Cookson, Klyne, and Shoppee, *Chem. and Ind.*, 1954, 21). With addition predominantly from the side remote from the isopropenyl group, these lead to ketols (XIV) and (XV) in proportion to (XII) and (XIII) provided the reaction is sufficiently rapid and is not

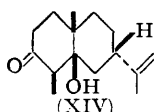
reversed. On conversion of the products into the fully conjugated ketones, measurement of rotation shows that the initial reaction is specific to the extent of better than 80% in favour of (XIV).



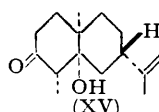
(XII)



(XIII)

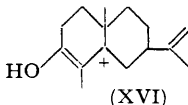


(XIV)

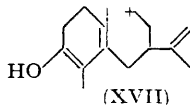


(XV)

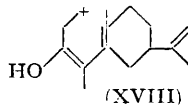
The racemisation process induced by the prolonged action of strong base and leading to equilibration of the isomers (VII) and (IX) has a parallel in the behaviour of the synthetic ketone (IV) towards 50% sulphuric acid noted above. The optical purity of the derived



(XVI)



(XVII)



(XVIII)

fully conjugated ketone was sensitive to the conditions of acid treatment and in particular to warming, which in one instance gave a fully conjugated ketone of $[\alpha]_{5461} +280.5^\circ$ from the optically pure ketone (IV). An acid-induced racemisation is understandable in terms of the species (XVI—XVIII) arising from protonation at the carboxyl group, and these observations may account for the partly racemic fully conjugated ketone obtained by Adamson *et al.* (*loc. cit.*).

EXPERIMENTAL

$[\alpha]_D$ are for solutions in CHCl_3 unless otherwise stated.

Condensation of (-)-Dihydrocarvone with Diethylmethyl-3-oxopentylammonium Iodide.—(a) *In ether.* Diethyl-3-oxopentylamine (51.2 g.) was treated with methyl iodide (46.5 g.) with cooling and rotation of the flask so as to deposit the methiodide on the walls. The sodio-derivative of (-)-dihydrocarvone (62 g.), made from sodamide (18 g.) under ether (700 c.c.), was then added under nitrogen and the mixture stirred in an ice-bath for 6 hr. Next morning the mixture was stirred and refluxed vigorously for 8 hr. The product isolated by addition of water, ether-extraction, and drying, gave on distillation (-)-dihydrocarvone (21.3 g.), followed by material (22.7 g.), b. p. 110—120°/0.1 mm., n_D^{20} 1.5220, which partly crystallised, to give (-)-*decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-isopropenyl-naphthalene* (3 g.). This formed prisms, m. p. 106° (from light petroleum), $[\alpha]_{5461} -54^\circ$ (c, 4.14) (Found: C, 76.1; H, 10.6. Calc. for $\text{C}_{15}\text{H}_{24}\text{O}_2$: C, 76.2; H, 10.2%). Adamson *et al.* (*loc. cit.*) give m. p. 103°. The bulk (14 g.) of the non-crystalline material on alumina (400 g.) gave (i) to light petroleum 2.8 g., (ii) to light petroleum-benzene 3.3 g., (iii) to benzene 2.8 g., and (iv) tenaciously held material, 4 g., removed by alcohol. The first fraction, after rechromatography, gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*octahydro-4 : 9-dimethyl-3-oxo-6-isopropenyl-naphthalene*, b. p. 91—94°/0.1 mm., n_D^{20} 1.5309, d_4^{20} 1.006, $[\alpha]_{5461} +70.4^\circ$, $[\alpha]_{5461} +58.2^\circ$ (c, 4.6), λ_{max} 251.5 μ ($\log \epsilon$ 4.1) (Found: C, 82.7; H, 10.0. Calc. for $\text{C}_{15}\text{H}_{22}\text{O}$: C, 82.6; H, 10.1%). This fraction gave an oxime, needles, m. p. 143° (from methanol), $[\alpha]_{5461} -25.4^\circ$ (c, 1.7 in EtOH), (Found: C, 77.3; H, 9.8. Calc. for $\text{C}_{15}\text{H}_{23}\text{ON}$: C, 77.3; H, 9.9%), and from the mother-liquors a second oxime as plates, m. p. 130° (from aqueous methanol), $[\alpha]_{5461} +78^\circ$ (c, 1.76 in EtOH) (Found: C, 77.3; H, 10.3%). The petroleum-benzene eluate (ii) on rechromatography with the same solvent gave fractions:

- (ii) a, 1.3 g., n_D^{20} 1.5322, $[\alpha]_{5461}$ (10 cm.) $+80^\circ$ (Found: C, 82.4; H, 10.0%)
 b, 0.5 g., n_D^{20} 1.5325, $[\alpha]_{5461}$ (10 cm.) $+93^\circ$ (Found: C, 81.9; H, 10.4%)
 c, 0.3 g., n_D^{20} 1.5326, $[\alpha]_{5461}$ (10 cm.) $+94^\circ$ (Found: C, 82.0; H, 10.3%)

i.e., corresponding to 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-*octahydro-4 : 9-dimethyl-3-oxo-6-isopropenyl-naphthalene*, but containing slightly more of the (+)-isomer. The alcohol eluate (iv) on distillation gave a substance, b. p. 120—130°/0.2 mm., n_D^{20} 1.5276, $[\alpha]_{5461} +13.7^\circ$ (c, 4.9) (Found: C, 76.4; H, 9.8. Calc. for $\text{C}_{15}\text{H}_{24}\text{O}_2$, *decahydro-4 : 9-dimethyl-10-hydroxy-3-oxo-6-isopropenyl-naphthalene*: C, 76.3; H, 10.2%).

(b) *In pyridine-ether.* Diethylmethyl-3-oxopentylammonium iodide (102 g.) in dry pyridine (125 c.c.) was added rapidly with stirring to the sodio-derivative from (-)-dihydrocarvone

(64 g.) and sodamide (18 g.) in ether (400 c.c.). The mixture was stirred at 0° for 12 hr., then heated under reflux for 5 hr. The product was distilled, giving (–)-dihydrocarvone (16.2 g.), followed by material of b. p. 140–150°/0.5 mm. (52.2 g.) which largely crystallised, to give (–)-decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene (27.7 g.), a further quantity (3.6 g.) of this ketol being obtained on further distillation and chromatography. From chromatography of the non-crystalline residue were obtained fractions: (i) (7.1 g.), b. p. 87–90°/0.1 mm., n_D^{20} 1.5252, $[\alpha]_{5461}^{20}$ (10 cm.) +42.2° (Found : C, 82.0; H, 10.2%); (ii) (4.5 g.), b. p. 91°/0.1 mm., n_D^{20} 1.5272, $[\alpha]_{5461}^{20}$ (10 cm.) +70.4° (Found : C, 81.8; H, 9.9%); (iii) (1 g.), b. p. 90–95°/0.1 mm., n_D^{20} 1.5014 (Found : C, 79.3; H, 10.7%).

Condensation of 2-Methylcyclohexanone with Diethylmethyl-3-oxopentylammonium Iodide.—

(i) *In ether.* The metho-salt (175.5 g.), treated with the sodio-ketone from 2-methylcyclohexanone (125 g.) and sodamide (23 g.) in ether (1 l.) and then as above, gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxonaphthalene (52 g.), b. p. 95–100°/0.5 mm., n_D^{20} 1.5197, followed by a small fraction which largely crystallised, to give *decahydro-10-hydroxy-4 : 9-dimethyl-3-oxonaphthalene* as prisms, m. p. 88°, from light petroleum (Found : C, 73.5; H, 10.4. $C_{15}H_{20}O_2$ requires C, 73.5; H, 10.2%). (ii) *In pyridine-ether.* The metho-salt (184 g.), added in dry pyridine (200 c.c.) to the sodio-2-methylcyclohexanone from sodamide (23 g.) and the ketone (120 g.) in ether (300 c.c.), gave 1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxonaphthalene (69 g.), b. p. 90–95°/0.5 mm., n_D^{20} 1.5272. By using ether-alcohol solution, Gunstone and Heggie (*loc. cit.*) obtained 46% of material, b. p. 99–100°/1 mm., n_D^{20} 1.5260.

Dehydration of (–)-Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene.—

(i) *With hydrochloric acid.* (–)-Decahydro-10-hydroxy-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene (7 g.) in ethyl alcohol (100 c.c.) was treated with concentrated hydrochloric acid (10 c.c.) and kept at room temperature for 60 hr. After neutralisation with sodium hydrogen carbonate solution the bulk of the alcohol was removed and the product, isolated by addition of water and ether, was distilled to give (+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene (6 g.), b. p. 91°/0.1 mm., n_D^{20} 1.5337, $[\alpha]_{5461}^{20}$ +210° (*c*, 3.5), λ_{max} 252 μ ($\log \epsilon$ 4.15 in alcohol) (Found : C, 82.4; H, 10.2. $C_{15}H_{20}O$ requires C, 82.6; H, 10.1%). The *oxime* formed prisms, m. p. 89–90° (from aqueous methanol), $[\alpha]_{5461}^{20}$ +233° (*c*, 1.05 in EtOH) (Found : C, 76.9; H, 10.0. $C_{15}H_{23}ON$ requires C, 77.3; H, 9.9%). The *semicarbazone* formed stout rhombs, m. p. 177° (from methanol), $[\alpha]_{5461}^{20}$ +244.2° (*c*, 1.1) (Found : C, 69.8; H, 9.3. $C_{16}H_{25}ON_3$ requires C, 69.8; H, 9.1%). The 2 : 4-dinitrophenylhydrazone formed scarlet prisms, m. p. 202°, from ethyl acetate (Found : C, 63.0; H, 6.5. $C_{21}H_{26}O_4N_4$ requires C, 63.3; H, 6.5%).

(ii) *With alcoholic potassium hydroxide.* The preceding "cyperone ketol" (3 g.) in 10% alcoholic potassium hydroxide (30 c.c.) was refluxed gently under nitrogen for 8 hr. After dilution with water and neutralisation by dilute hydrochloric acid the product was isolated by means of ether and distilled, to give (+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-octahydro-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene (2.5 g.), b. p. 92°/0.1 mm., n_D^{20} 1.5343, $[\alpha]_{5461}^{20}$ +216.8° (*c*, 2.2), λ_{max} 252 μ ($\log \epsilon$ 4.23) (Found : C, 82.6; H, 10.4. Calc. for $C_{15}H_{20}O$: C, 82.6; H, 10.1%). This gave the same oxime and semicarbazone as the preparation above.

(iii) The "cyperone ketol" (0.2 g.) in benzene (5 c.c.) with pyridine and piperidine (10 drops each) was recovered quantitatively, having b. p. 110–115°/0.05 mm., m. p. 106°, after 100 hours' refluxing. The same experiment, with alcohol as solvent and 20 hours' refluxing, gave a product which very largely crystallised and from which the ketol was recovered in good yield, m. p. 106°, from light petroleum.

(+)-Decahydro-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene.—(+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-Octahydro-4 : 9-dimethyl-6-isopropenylnaphthalene in alcohol with 20% palladised charcoal took up ~2 mols. of hydrogen, to give a product, b. p. 85–90°/0.05 mm., which mainly crystallised and by chromatography on alumina gave in the first light petroleum eluates (+)-decahydro-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene as prisms, m. p. 96° (from light petroleum), $[\alpha]_{5461}^{20}$ +25.8° (*c*, 1.74) (Found : C, 81.0; H, 12.0. $C_{15}H_{26}O$ requires C, 81.1; H, 11.7%). The 2 : 4-dinitrophenylhydrazone formed yellow-orange prisms, m. p. 169°, from ethyl alcohol-ethyl acetate (Found : C, 62.5; H, 7.7. $C_{21}H_{30}O_4N_4$ requires C, 62.6; H, 7.5%).

(+)-Decahydro-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene.—(+)-1 : 2 : 3 : 5 : 6 : 7 : 8 : 9-Octahydro-4 : 9-dimethyl-3-oxo-6-isopropenylnaphthalene (0.5 g.) in dry ether (20 c.c.) was added to a solution of lithium (0.1 g.) in liquid ammonia (150 c.c.) and after 0.5 hr. ammonium chloride (2 g.) was added and the ammonia allowed to evaporate. Recovered by addition of water and ether, the product formed an oil, b. p. 95°/0.1 mm., which crystallised to give *decahydro-4 : 9-di-*

methyl-3-oxo-6-isopropenylnaphthalene, prisms, m. p. 48° (from light petroleum), $[\alpha]_{5461} + 25.9^\circ$ (*c*, 3.21) (Found: C, 81.4; H, 11.4. $C_{15}H_{24}O$ requires C, 81.8; H, 10.9%). The 2:4-dinitrophenylhydrazone formed orange-yellow prisms, m. p. 192°, from alcohol (Found: C, 63.0; H, 7.4. $C_{21}H_{28}O_4N_4$ requires C, 63.0; H, 7.0%).

(+)-1:2:3:7:8:9-Hexahydro-4:9-dimethyl-3-oxo-6-isopropyl-naphthalene.—(i) (-)-Decahydro-10-hydroxy-4:9-dimethyl-6-isopropenylnaphthalene (0.4 g.) was treated with cold 50% v/v sulphuric acid (5 c.c.) and after 4 hr. the yellow solution was diluted with water and ice. The product recovered by means of ether and washing with water gave (+)-1:2:3:7:8:9-hexahydro-4:9-dimethyl-3-oxo-6-isopropyl-naphthalene, b. p. 90—95°/0.1 mm., n_D^{20} 1.5632, λ_{max} 301 m μ ($\log \epsilon$ 4.44 in EtOH), $[\alpha]_{5461} + 678^\circ$ (*c*, 1.44), $+672^\circ$ (*c*, 4.5) (Found: C, 82.7; H, 10.0. $C_{15}H_{22}O$ requires C, 82.6; H, 10.1%). The oxime formed prisms, m. p. 139° (from aqueous methanol), $[\alpha]_{5461} + 307^\circ$ (*c*, 1.9 in EtOH) (Found: C, 77.5; H, 10.1. $C_{15}H_{23}ON$ requires C, 77.3; H, 9.9%). The semicarbazone formed yellow (chromotropic) prisms, m. p. 208° (from methanol), $[\alpha]_{5461} + 401^\circ$ (*c*, 1.08) (Found: C, 69.8; H, 9.3. $C_{16}H_{25}ON_3$ requires C, 69.8; H, 9.1%). The "β-ketone" and derivatives described by Adamson, McQuillin, Robinson, and Simonsen (*loc. cit.*) were partly racemic but the melting point of the ketol used was also somewhat low.

(ii) (+)-1:2:3:5:6:7:8:9-Octahydro-4:9-dimethyl-3-oxo-6-isopropenylnaphthalene, $[\alpha]_{5461} + 210^\circ$ (1 g.), in 50% v/v sulphuric acid (10 c.c.), as above, gave a (+)-1:2:3:7:8:9-hexahydro-4:9-dimethyl-3-oxo-6-isopropyl-naphthalene, b. p. 95°/0.1 mm., n_D^{20} 1.5635, $[\alpha]_{5461} + 539^\circ$ (*c*, 2.5) (Found: C, 82.8; H, 10.1. Calc. for $C_{15}H_{22}O$: C, 82.6; H, 10.1%).

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