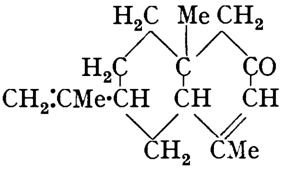
146. *The Constitutions of Eremophilone, Hydroxyeremophilone, and Hydroxydihydroeremophilone. Part II.*

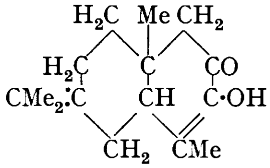
By A. E. BRADFIELD, N. HELLSTRÖM, A. R. PENFOLD, and J. L. SIMONSEN.

The observation (J., 1936, 667; 1937, 760) that tetrahydroeremophilone after treatment with methylmagnesium iodide and selenium dehydrogenation gave 1 : 5-dimethyl-7-*iso*propylnaphthalene and not 1 : 3-dimethyl-7-*iso*propylnaphthalene showed that the structure (I) could not correctly represent eremophilone. The difficulties involved by placing the carbonyl group of the ketone at position 5 are discussed and the conclusion is reached that, although dihydroeremophilol yields eudalene on selenium dehydrogenation, it cannot have an angle methyl group at position 9. An attempt has been made to determine the structure of hydroxyeremophilone, previously represented by (II), by a detailed investigation of its oxidation products and it is now found that one of these is a *keto-acid*, $C_{10}H_{16}O_3$. This suggested that the benzoate of hydroxyeremophilone might be (VII); the keto-acid would then be (IX). The latter acid should yield on reduction 2 : 2-dimethyl*cyclo*hexylacetic acid. Comparison with a synthetic specimen of this acid has shown this to be incorrect. The benzoate, therefore, cannot have the structure (VII) unless a molecular rearrangement has occurred during its degradation. Alternative formulæ for eremophilone and its congeners are discussed, but a final decision must await further experiments.

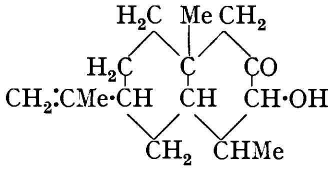
IT was suggested (Bradfield, Penfold, and Simonsen, J., 1932, 2744) that the three ketones, eremophilone, hydroxyeremophilone, and hydroxydihydroeremophilone, which occur together in the oil from the wood of *Eremophila Mitchelli*, were represented respectively by (I), (II), and (III). Before presenting the evidence which now leads us to reject these formulæ it is necessary to summarise briefly the grounds upon which they were based.



(I.)



(II.)



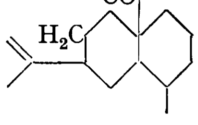
(III.)

(A) *Eremophilone.* (i) The ketone contains two ethylenic linkages (catalytic hydrogenation). (ii) Dihydroeremophilol gives on selenium dehydrogenation eudalene and on ozonolysis formaldehyde and a keto-alcohol, $C_{14}H_{24}O_2$. From the latter a hydroxy-acid, $C_{13}H_{22}O_3$, was obtained by further oxidation with sodium hypobromite, thus proving conclusively the presence of an *iso*propenyl side chain in dihydroeremophilol. (iii) Eremophilone must contain the group — $CH_2{\cdot}CO{\cdot}CH{:}CH$ —. The presence of the methylene group was proved by the preparation of a crystalline hydroxymethylene derivative. Conjugation of the ethylene linkage with the carbonyl group was established (*a*) by the preparation of a compound with hydrogen sulphide, (*b*) by oxidation with hydrogen peroxide in alkaline solution to an oxide, eremophilone oxide (cf. Weitz and Scheffer, *Ber.*, 1921, **54**, 2327), and (*c*) the absorption spectrum (Gillam, J., 1936, 676).

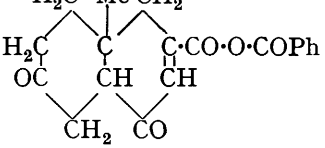
(B) *Hydroxyeremophilone.* (i) The hydroxy-ketone can be prepared from eremophilone oxide. (ii) On ozonolysis it gives acetone with only a trace of formaldehyde, thus proving the presence of an *iso*propylidene group. (iii) Oxidation with hydrogen peroxide in alkaline solution yields, together with other products, two isomeric dibasic acids, $C_{15}H_{26}O_6$, suggesting the presence of a potential 1 : 2-diketone.

(C) *Hydroxydihydroeremophilone.* (i) The keto-alcohol gave on catalytic hydrogenation hydroxytetrahydroeremophilone, from which tetrahydroeremophilone was prepared by reduction with sodium amalgam, thus proving the relative positions of the hydroxyl and the carbonyl group. (ii) Ozonolysis gave formaldehyde (*iso*propenyl group), and with hydrogen peroxide in alkaline solution one of the isomeric dibasic hydroxy-acids, $C_{15}H_{26}O_6$, previously prepared from hydroxyeremophilone, was obtained.

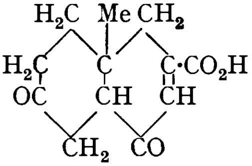
Recently, during the investigation of the structure of the sesquiterpene ketone, α-cyperone (J., 1936, 667; 1937, 760), we had occasion to investigate the action of methylmagnesium iodide on tetrahydroeremophilone and on selenium dehydrogenation of the product we obtained 1 : 5-dimethyl-7-*iso*propylnaphthalene in place of 1 : 3-dimethyl-7-*iso*propylnaphthalene. This showed, assuming no migration of the methyl groups at any stage, that in eremophilone the carbonyl group was in position 5, and not 3 as had been previously assumed. Evidence in support of this orientation was furnished by the fact that hydroxymethylene-eremophilone gave on reduction and dehydrogenation 1 : 6-dimethyl-7-*iso*propylnaphthalene. These experiments are satisfactorily accounted for only if we assign to eremophilone the skeleton structure (IV). Such a representation does not, however, permit of the conjugation of an ethylenic linkage with the carbonyl group, for which irrefutable evidence [see (A) above] has been provided. It became necessary, therefore, to subject the whole of the experimental evidence previously advanced to a critical revision, and a promising line of attack appeared to us to lie in a more detailed study of the degradation of hydroxyeremophilone.



(IV.)



(V.)



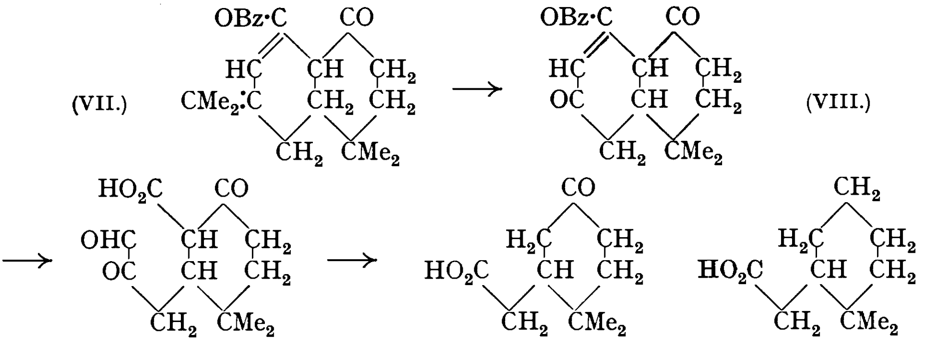
(VI.)

We recorded (*loc. cit.*, p. 2755) that when the benzoate of hydroxyeremophilone was ozonised it gave, in addition to acetone, a crystalline product, m. p. 186—188°, which we considered to have the composition $C_{19}H_{18}O_5$ and represented as the anhydride (V), since on digestion with alkali it gave benzoic acid and a keto-acid, analysed as the semicarbazone, m. p. 215—216°, and represented by (VI). It was, however, necessary to make the assumption that the semicarbazone crystallised with two molecules of alcohol of crystallisation.

We now find that the oxidation of the benzoate proceeds in a more complex manner than had been assumed and a further study of the products of this oxidation, together with the oxidation of hydroxyeremophilone and its methyl ether, has afforded a partial explanation of the fallacy underlying our previous conclusions.

When the benzoate is ozonised until the issuing gases just show the presence of ozone, the crystalline " anhydride " previously described, together with unchanged benzoate, can be readily isolated. As was mentioned (*loc. cit.*, p. 2755), this oxidation product is somewhat unstable and it tends to decompose on prolonged boiling with alcohol. It can be much more readily purified by crystallisation from ethyl acetate and analysis has shown that it contains two more hydrogen atoms than had been assumed previously and that it has the composition $C_{19}H_{20}O_5$. Its structure is discussed later (p. 769). If, however, the ozonolysis of the benzoate is prolonged, this crystalline product can no longer be isolated, the main product of the oxidation being a keto-acid, yielding the semicarbazone, m. p. 215—216°, referred to above. The analytical figures for carbon and hydrogen previously obtained have been confirmed, but a nitrogen estimation has shown that the semicarbazone has the composition $C_{11}H_{19}O_3N_3$. This composition is supported by hydrolysis of the semicarbazone to the parent *keto-acid*, $C_{10}H_{16}O_3$, m. p. 105—107°, an acid formed also in small amount when the " anhydride " is treated with alkali. This acid can be prepared by the oxidation of hydroxyeremophilone with chromic acid and by the ozonolysis of its methyl ether.

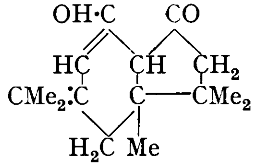
It is clearly very difficult to reconcile the formation of a keto-acid having this composition with the assignment to hydroxyeremophilone of a structure containing an angle methyl group in the 9-position, an assumption usually made in the case of sesquiterpene derivatives yielding eudalene on dehydrogenation. On the basis of the isoprene theory the most probable representation for the benzoate appeared to be (VIII); the keto-acid would then be (IX), the oxidation proceeding in accordance with the scheme:



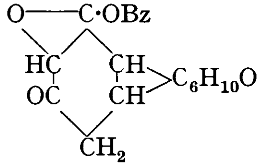
(VII.) (VIII.) (IX.) (X.)

Reduction (Clemmensen) of the keto-acid gave a liquid acid, $C_{10}H_{18}O_2$, yielding a dextrorotatory p-*phenylphenacyl* ester, m. p. 65—67°, which, were the above reasoning correct, should be a derivative of *d*-2 : 2-dimethyl*cyclo*hexylacetic acid (X). This acid was therefore synthesised, but its *p*-phenylphenacyl ester (this vol., p. 776) was not identical with that prepared from the acid obtained by the degradation of the benzoate. The latter substance cannot therefore be represented by (VII) unless a wandering of a methyl group occurs during the Clemmensen reduction of the keto-acid (IX) or at some prior stage in the degradation.

An alternative structure for hydroxyeremophilone, also in accordance with the facts outlined above, is (XI), which contains three isoprene nuclei united in a somewhat unusual manner. Its conversion into eudalene on selenium dehydrogenation would involve the elimination of an angle methyl group, coupled with ring widening at the *gem*-dimethyl group.



(XI.)



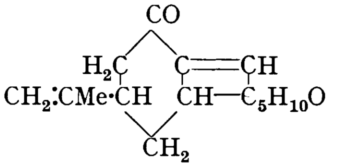
(XII.)

Our knowledge of the molecular rearrangements which may occur on selenium dehydrogenation is still limited (cf. Linstead, *Ann. Reports*, 1936, 294; Chatterjee, *J. Indian Chem. Soc.*, 1936, **13**, 588), so the possibility of this rearrangement cannot be rejected.

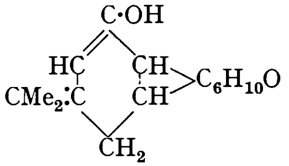
The structure of the crystalline "anhydride," m. p. 186—188°, has not been proved, but we suggest that it is the oxide (XII) formed by the action of hydrogen peroxide on the primary product (VIII) of the ozonolysis.

A further unusual product of the ozonolysis of the benzoate was an *acid*, $C_7H_6O_4$, m. p. 230—232°. This acid, which was comparatively stable and could be esterified with either diazomethane or methyl sulphate to give a liquid methyl ester yielding the original acid on alkaline hydrolysis, is probably a moloxide of benzoic acid, since it gives this acid in quantitative yield on sublimation in a low vacuum.

Although, therefore, the experiments outlined above have not enabled us to elucidate in their entirety the structures of eremophilone and hydroxyeremophilone, we think



(XIII.)



(XIV.)

that there can be no doubt that eremophilone and hydroxyeremophilone must contain the skeletons (XIII) and (XIV) respectively. In the latter formula the carbonyl group of eremophilone is represented as enolising to give the hydroxy-group of hydroxyeremophilone. This is in accord with the complete conversion of the *iso*propenyl group in the former into an *iso*propylidene group in the latter occasioned by conjugation of the ethylenic linkages. We may note here also that any structure for hydroxydihydroeremophilone must permit of the enolisation of the carbonyl group, since the presence of two acetyl groups in the diacetate previously described (*loc. cit.*, p. 2757) has been confirmed by analysis. Furthermore, the ethylenic linkages in eremophilone cannot be conjugated, since the hydrocarbon, prepared from the semicarbazone of the ketone by the Wolff–Kishner reaction, cannot be reduced by sodium and alcohol.

It was mentioned above that when hydroxyeremophilone was oxidised with chromic acid the keto-acid $C_{10}H_{16}O_3$ was obtained. A further product of the oxidation is a *substance*, $C_{12}H_{18}O_3$, m. p. 193—194·5°, which has pseudo-acidic properties and has been characterised by the preparation of an *acetate*, m. p. 164—165°, and a *methyl* ether, m. p. 121—122°. The phenol gives no colour with ferric chloride and it does not appear to react with carbonyl reagents. We have obtained no clue to its structure, since it yields no recognisable degradation products. It is formed also by the ozonolysis of hydroxyeremophilone and its methyl ether.

We have reinvestigated the catalytic hydrogenation of hydroxyeremophilone benzoate (*loc. cit.*, p. 2757) and we now find that the product is not homogeneous. If the reduced benzoate is hydrolysed and the product distilled, an oil is obtained which partly crystallises. The solid, m. p. 89—90°, has the composition $C_{15}H_{24}O_2$ and it is therefore isomeric with hydroxydihydroeremophilone. It differs from this substance in giving an intense ferric chloride coloration and we suggest that it be designated β-*hydroxydihydroeremophilone.* It is probable that it still contains the enolic hydroxy-group present in hydroxyeremophilone, the exocyclic ethylenic linkage having been reduced. It is somewhat unstable, becoming gummy on keeping—a change which does not appear to be due solely to oxidation, since it proceeds also in the absence of air. It gives on oxidation with hydrogen peroxide in alkaline solution a liquid acid. The liquid from which β-hydroxydihydroeremophilone had been separated and which, from its colour with ferric chloride, still contained much of this substance, was oxidised with hydrogen peroxide in alkaline solution; it then gave a small quantity of a crystalline *acid*, $C_{15}H_{26}O_4$, m. p. 193—195°. A further product of the oxidation was a *phenolic oxide*, $C_{15}H_{24}O_3$, m. p. 136—137°.

During these experiments we have devised a more convenient method for the separation of eremophilone and hydroxyeremophilone and we have obtained evidence of the presence in the oil of a fourth ketone having the composition $C_{15}H_{22}O$. It is present in the lower-boiling fractions, but it could not be obtained free from eremophilone. It was characterised by the preparation of a 2 : 4-*dinitrophenylhydrazone*, m. p. 155—156·5°.

EXPERIMENTAL.

Separation of Eremophilone and Hydroxyeremophilone.—The crude oil from *E. Mitchelli* (200 g.) was dissolved in pyridine (400 c.c.) and to the cooled solution benzoyl chloride (112 g.) was gradually added. After being kept overnight, the mixture was poured on ice and dilute sulphuric acid, the oil dissolved in ether, and the ethereal solution washed with dilute sulphuric acid, sodium hydroxide solution, and water, and dried. The viscid gum (280 g.) left on removal of the solvent was dissolved in ligroin (b. p. 40—60°) (500 c.c.) and, after inoculation with hydroxyeremophilone benzoate, kept in the ice-box for 48 hours. The benzoate (52 g.), which had separated, was collected, and the filtrate, after removal of the ligroin, distilled at 3 mm., two fractions being collected: (i) up to 190° and (ii) 190—250°.

Fraction (i) was dissolved in ether, washed with sodium carbonate solution to remove benzoic acid, dried, recovered (72 g.), and distilled, the main fraction having b. p. 170—180°/20 mm. This partly crystallised; the solid eremophilone was collected, and the filtrate repeatedly fractionated, the crystalline eremophilone which separated from the higher-boiling fractions being removed. Ultimately the following fractions (at 11 mm.) were obtained: (*a*) b. p. up to 140°; (*b*) 140—150°; (*c*) 160—163°, mainly 155—158°, and (*d*) 163—168°. Fraction (*d*) crystallised and consisted essentially of eremophilone. From fraction (*c*), which formed the main fraction of lower boiling point, and also from fraction (*b*), a 2 : 4-*dinitro-*

phenylhydrazone was prepared which crystallised from alcohol in fine yellow needles, m. p. 155—156·5° (Found: C, 63·3; H, 6·4. $C_{21}H_{26}O_4N_4$ requires C, 63·3; H, 6·5%). The ketone corresponding to this dinitrophenylhydrazone could not be completely freed from eremophilone, as was shown by the fact that all the fractions gave with hydrogen peroxide in the presence of alkali small amounts of eremophilone oxide (this may possibly provide a method for the separation of the two ketones). The ketone gave a gummy semicarbazone and attempts to regenerate it from its dinitrophenylhydrazone failed.

Fraction (ii) (see above) was dissolved in ether, washed with sodium carbonate solution to remove benzoic acid, recovered (110 g.), and dissolved in ligroin (b. p. 40—60°) (200 c.c.); on keeping, a further quantity of hydroxyeremophilone benzoate (19 g.) separated. The oil soluble in ligroin was not further examined, but it probably contained the benzoate of hydroxydihydroeremophilone.

Hydrocarbon from Eremophilonesemicarbazone.—The semicarbazone (6 g.) was heated with sodium ethoxide (alcohol, 10 c.c.; sodium, 0·75 g.) at 210° for 6 hours. The hydrocarbon (3 g. from 18 g. of the semicarbazone) had b. p. 130°/13 mm. On titration with perphthalic anhydride (Böhme, *Ber.*, 1937, **70**, 379) it showed the presence of two ethylenic linkages and the titration value was unchanged after attempted reduction with sodium and alcohol.

Conversion of Hydroxymethylene-eremophilone into 1 : 6-*Dimethyl*-7-iso*propylnaphthalene.*—The mixture of solid (2·3 g.) and oil (*ca.* 6 g.) from the preparation of hydroxymethylene-eremophilone in methyl alcohol (150 c.c.) was shaken in hydrogen at 3 atm. pressure in the presence of a palladium–norit catalyst. The absorption of hydrogen was slow and ceased after 1350 c.c. had been taken up (calc., 3000 c.c.). Methyl alcohol was removed from the filtered solution by distillation through a column, and the residue, after drying in ethereal solution, further reduced with alcohol (200 c.c.) and sodium (20 g.). The recovered oil (4·5 g.) was heated with selenium (7 g.) at 300° for 40 hours and then at 320° for 12 hours. The somewhat tarry product was extracted with ether, the extract washed with sodium hydroxide solution, and dried, and the ether removed. The oil obtained (1·3 g.) gave a small yield of a picrate, which after crystallisation from alcohol had m. p. 123—125° both alone and in admixture with 1 : 6-dimethyl-7-*iso*propylnaphthalene picrate.

Hydroxyeremophilone.—Hydroxyeremophilone, prepared by the hydrolysis of the benzoate with alcoholic potassium hydroxide, was purified by distillation under diminished pressure, followed by crystallisation from methyl alcohol. Unlike the specimen described previously (*loc. cit.*, p. 2755), it gave correct figures on analysis (Found: C, 76·9; H, 9·4. Calc. for $C_{15}H_{22}O_2$: C, 76·9; H, 9·4%). Numerous attempts were made to establish the presence of a carbonyl group in the hydroxy-compound itself, the benzoate, and the acetate, m. p. *ca.* 55°, b. p. 210—211°/25 mm., but were all unsuccessful. With Brady's reagent an amorphous precipitate slowly formed, which could not be crystallised. The benzoate did not react with methylmagnesium iodide.

Hydroxyeremophilone Methyl Ether.—The alcohol (14 g.) in acetone (100 c.c.) was treated with methyl sulphate (10 c.c.) and aqueous sodium hydroxide (20 c.c.; 30%), the solution being kept just alkaline (mechanical stirring). A deep red colour developed at first, changing gradually to a pale yellow. After being kept overnight, the mixture was heated on the water-bath for 1 hour, cooled, and diluted with water, and the oil, which separated, dissolved in ether. The ethereal extract was washed successively with sodium hydroxide solution, dilute sulphuric acid, and water, and dried, and the solvent removed. The *methyl* ether (14·5 g.) was a faintly yellow oil, b. p. 180°/13 mm. (Found: C, 77·4; H, 9·7. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%). Hydroxyeremophilone does not react with diazomethane. The methyl ether, which gave no colour with ferric chloride, could not be reduced with aluminium *iso*propoxide. On treatment with *iso*amyl formate in ethereal solution in the presence of sodium an oil, soluble in alkali, was obtained, which gave with alcoholic ferric chloride a deep red coloration. The oil reacted at once with carbonyl reagents, but the derivatives were amorphous. Amorphous products were obtained also by the interaction of the methyl ether with piperonal and *m*-nitrobenzaldehyde.

β-*Hydroxydihydroeremophilone.*—Hydroxyeremophilone benzoate (23 g.) in ethyl acetate was reduced under pressure (3 atm.) in the presence of a palladium–norit catalyst; absorption of hydrogen was very slow and ceased completely after slightly more than 1 mol. of hydrogen had been taken up. Removal of the solvent from the filtered solution left a viscid gum, which was hydrolysed with methyl-alcoholic potassium hydroxide solution; addition of water then precipitated an oil. This was isolated by ether in the usual manner; the residue (13 g.) remaining after removal of the solvent partly crystallised and had b. p. 169—172°/13 mm.

From the semi-solid distillate, which gave an intense green colour, changing to blue, with alcoholic ferric chloride, the solid was separated. β-*Hydroxydihydroeremophilone* crystallised from dilute methyl alcohol in slender prisms, m. p. 89—90°, $[\alpha]_{5461} + 42°$ in methyl alcohol (*c*, 2·07) (Found : C, 76·3; H, 10·1. $C_{15}H_{24}O_2$ requires C, 76·3; H, 10·2%). The solid gave the same colour reactions with ferric chloride as the oil.

The oil (6·5 g.), b. p. 165—167°/12 mm., from which the solid had been separated was dissolved in methyl alcohol (45 c.c.) and treated with a mixture of sodium hydroxide solution (4N; 12 c.c.) and hydrogen peroxide (11%; 31 c.c.). No heat was generated and after 1 hour the mixture was heated at 50°; a vigorous reaction then ensued, sufficient heat being generated to maintain this temperature for 30 minutes. After 12 hours water was added, the neutral oil (3 g.) removed by ether, and the solution acidified and extracted with ether. The ethereal extract was washed with sodium carbonate and then with sodium hydroxide solution. From the latter, carbon dioxide precipitated a *phenol*, which crystallised from dilute methyl alcohol in long prismatic needles, m. p. 136—137°, giving an olive-green ferric chloride coloration (Found : C, 71·5; H, 9·4. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%). From the sodium carbonate solution, an acid (4·5 g.) was isolated which partly crystallised on trituration with formic acid. The crystalline *acid* separated from methyl alcohol (50%) in soft needles, m. p. 193—195° (Found : C, 66·5; H, 9·4; *M*, 278. $C_{15}H_{26}O_4$ requires C, 66·7; H, 9·6%; *M*, 270). The acid appeared to be stable to potassium permanganate in alkaline solution and it gave with acetyl chloride a liquid anhydride.

Oxidation of Hydroxyeremophilone and its Derivatives.—(a) *Ozonolysis of hydroxyeremophilone*. The ketone (5 g.) in ethyl acetate (25 c.c.) was treated with ozone at 0° until the gas passed through freely. The solvent was removed from the deep yellow solution under diminished pressure and after the addition of water (10 c.c.) the ozonide was decomposed by heating on the water-bath for 1 hour. Sodium carbonate was added, the insoluble oil dissolved in ether, the ethereal extract washed with sodium hydroxide solution (B), and the solvent removed. The residue (0·4 g.) was unchanged hydroxyeremophilone. Acidification of the sodium hydroxide solution (B) precipitated a solid (1·2 g.), which crystallised from methyl alcohol (70%) in thin plates, m. p. 191—192°, both alone and after admixture with the phenol obtained from the oxidation of hydroxyeremophilone with chromic acid (see below). The identity was confirmed by the preparation of the acetyl derivative, m. p. 164—165°.

The sodium carbonate solution on acidification gave a gummy acid (3·2 g.). This reacted with carbonyl reagents to give amorphous products and on oxidation with sodium hypobromite gave a small amount of bromoform.

(b) *Oxidation of hydroxyeremophilone with chromic acid.* To a solution of the ketone (6·2 g.) in acetic acid (50 c.c.), chromic acid (7 g.) in acetic acid (40 c.c.) and water (10 c.c.) was added during 8 hours (mechanical stirring). After the addition of water (50 c.c.) the excess of chromic acid was removed by sulphur dioxide, and the greater part of the acetic acid distilled off with steam. The cooled residue from the steam distillation, after saturation with ammonium sulphate, was extracted with ether, and the extract washed with sodium hydroxide solution, dried, and evaporated, a small amount of hydroxyeremophilone being recovered. Saturation of the sodium hydroxide solution with carbon dioxide precipitated a phenol (1·2 g.), the filtrate (*A*) being reserved. The *phenol* crystallised from dilute methyl alcohol in thin plates or prisms, m. p. 193—194·5° (Found : C, 68·3; H, 8·4. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·6%). It gave in alkaline solution with sodium hypobromite an immediate precipitate of bromoform, but the acid product of the oxidation could not be characterised. The *acetyl* derivative, prepared by digestion of the phenol with acetic anhydride containing a trace of pyridine, crystallised from methyl alcohol in well-formed prisms m. p. 164—165° (Found : C, 66·7; H, 7·9. $C_{14}H_{20}O_4$ requires C, 66·7; H, 7·9%). The *methyl* ether, prepared by the action of methyl sulphate, crystallised from methyl alcohol in hexagonal prisms, m. p. 121—122° (Found : C, 69·3; H, 8·5. $C_{13}H_{20}O_3$ requires C, 69·6; H, 8·9%).

The sodium carbonate solution (*A* above), from which the phenol had been separated, was acidified and extracted with ether. The liquid residue remaining after removal of the solvent was triturated with sodium bicarbonate solution, which left undissolved a further quantity of the phenol (0·4 g.); the filtered solution was again acidified and extracted with ether Evaporation of the dried ethereal extract left an oil (1 g.), which formed a sparingly soluble *semicarbazone*. This crystallised from alcohol in well-formed prisms, decomp. 207—208° or, when rapidly heated, 215—216° (Found : C, 54·7; H, 8·1; N, 17·9. $C_{11}H_{19}O_3N_3$ requires C, 54·8; H, 7·9; N, 17·4%). Hydrolysis of the semicarbazone with sulphuric acid (10%) gave the *keto-acid*, which crystallised from dilute methyl alcohol in prismatic needles,

m. p. 105—107° (Found: C, 65·0; H, 8·6. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%). The acid is identical with that prepared by the ozonolysis of hydroxyeremophilone benzoate (see below).

(c) *Ozonolysis of hydroxyeremophilone methyl ether.* The ether (7 g.) in methyl acetate (50 c.c.) was ozonised at 0°. After decomposition of the ozonide the oil was dissolved in ether, and the ethereal extract washed successively with sodium carbonate and sodium hydroxide solutions. Evaporation of the dried extract gave hydroxyeremophilone methyl ether (2 g.). The sodium carbonate solution gave on acidification an acid (4·5 g.), from which the semicarbazone (0·6 g.) referred to above was prepared. The non-ketonic fraction of the acid was not further examined. From the sodium hydroxide solution, the phenol (0·5 g.) was isolated.

(d) *Ozonolysis of hydroxyeremophilone benzoate.* (i) The benzoate (2 g.) in carbon tetrachloride (20 c.c.) was ozonised at 0° until ozone was present in the issuing gases. After removal of the solvent from the deep yellow solution the ozonide in water (10 c.c.) was heated on the water-bath for 1 hour and then on the sand-bath for ½ hour. After cooling, the water was decanted from the resin, which, on shaking with ether, gave a crystalline solid (A) (0·7 g.). The ethereal extract was washed with sodium carbonate solution, which removed some benzoic acid, with sodium hydroxide solution (B), and the solvent removed, the residue (0·6 g.) being unchanged benzoate.

The solid (A), m. p. 175°, was recrystallised from alcohol (three times) and finally from ethyl acetate, from which it separated in long prismatic needles, m. p. 186—188° (Found: C, 69·5; H, 6·0. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·0%). The *oxide*, on hydrolysis with alcoholic potassium hydroxide solution, gave a small quantity of the keto-acid, $C_{10}H_{16}O_3$, characterised by the preparation of its semicarbazone, decomp. 207—208°.

The sodium hydroxide solution (B) gave, on acidification, a gum (0·3 g.) giving a deep red ferric chloride coloration. A semicarbazone was prepared which crystallised from methyl alcohol in prisms, m. p. 166° (Found: 61·3; H, 6·5%). This was not identified.

(ii) The benzoate (3 g.) in ethyl acetate (30 c.c.) was ozonised at 0° until an excess of ozone had passed through the solution for at least 4 hours. The yellow solution, which still contained a trace of undissolved benzoate, was filtered, and the solvent removed under diminished pressure. After decomposition with water on the water-bath the semicrystalline oil was dissolved in ether (oxalic acid was present in the aqueous solution) and the ethereal solution washed with sodium hydroxide solution. Evaporation of the solvent left a solid (0·1 g.) consisting of unchanged benzoate. The sodium hydroxide solution, after the addition of hydrogen peroxide (100-vol., 1 c.c.), was kept overnight, acidified, and extracted with ether; the dried ethereal extract on evaporation left an oil (2·8 g.). This was treated with an aqueous solution of semicarbazide acetate, a crystalline semicarbazone (1·7 g.) being rapidly deposited. This was collected and washed with ether, and the filtrate reserved. The semicarbazone crystallised from alcohol in prisms, decomp. 208—209°, and was identical with that prepared from the acid obtained by the oxidation of hydroxyeremophilone with chromic acid (see above). The *keto-acid*, obtained by hydrolysis of the semicarbazone with dilute sulphuric acid, crystallised from ligroin (b. p. 100—120°) or dilute methyl alcohol in needles, m. p. 105—107°, $[\alpha]_{5461}$ + 28·27° in methyl alcohol (*c*, 4·364) (Found: C, 65·2; H, 8·6. $C_{10}H_{16}O_3$ requires C, 65·2; H, 8·7%). The acid was sparingly soluble in cold water, somewhat readily in hot, and readily soluble in most of the ordinary organic solvents. It was stable to potassium permanganate in alkaline solution.

The solution from which the semicarbazone had been separated was repeatedly extracted with ether and this extract, combined with the ethereal washings from the semicarbazone, was, after removal of the solvent, distilled in steam. This removed benzoic acid; the cooled residue from the distillation was, after saturation with ammonium sulphate, extracted with ether. Removal of the solvent left a crystalline acid (0·2 g.). The *moloxide* of benzoic acid crystallised from water in needles, decomp. 230—232° after sintering at 200°. Two different specimens were analysed (Found: C, 54·2, 54·9; H, 3·7, 3·4. $C_7H_6O_4$ requires C, 54·5; H, 3·9%).

Reduction of the Keto-acid.—The keto-acid (1·7 g.), amalgamated zinc (20 g.), and hydrochloric acid (15 c.c.) were heated under reflux for 6 hours, a further quantity of acid (20 c.c.) then added, and the heating continued for 12 hours. From the cooled solution, ether extracted a liquid acid (1·4 g.) which was readily volatile in steam. To remove a little unchanged keto-acid, the oil was dissolved in ligroin (b. p. 40—60°), the solution filtered, and the ligroin removed. From the liquid acid, a p-*phenylphenacyl* ester was prepared which crystallised from methyl alcohol in rosettes of leaflets, m. p. 65—67°, $[\alpha]_{5461}$ + 15·3° in ethyl acetate (*c*, 1·026) (Found : C, 78·9; H, 7·4. $C_{24}H_{28}O_3$ requires C, 79·1; H, 7·7%).

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