

LXVI.—*Morindone*.

By JOHN LIONEL SIMONSEN.

DURING the past few years, owing to the shortage of synthetic dyes, the use of natural colouring matters has, to some extent, been revived, and it appeared, therefore, to be a matter of some interest to attempt to elucidate the constitution of the main constituent of *Morinda citrifolia* and *M. umbellata*, morindone, since the root bark of this tree at one time found considerable application in India for the dyeing of cloth.

Morindone occurs in the root bark mainly in the form of the glucoside, morindin, although a small quantity of the free colouring matter is present in the bark. Morindin appears to have been first isolated from *M. citrifolia* by Anderson (*Annalen*, 1849, **71**, 216). He ascribed to it the formula $C_{28}H_{30}O_{15}$, and by sublimation obtained a substance resembling alizarin in its properties, to which he gave the name morindone. Subsequent investigators appear to have regarded morindin as identical with ruberythric acid and morindone as identical with alizarin. Thorpe and Greenall (T., 1887, **51**, 52), and later Thorpe and Smith (T., 1888, **53**, 171), using *M. citrifolia* as the source of their material, proved conclusively, however, that morindone possessed the formula $C_{15}H_{10}O_5$, and were of the opinion that morindin was more correctly represented by the formula $C_{26}H_{28}O_{14}$ than by the formula suggested by Anderson. They further considered morindone to be a trihydroxymethylanthraquinone.

The presence of morindin and morindone in *M. umbellata* was first proved by Perkin and Hummel (T., 1894, **65**, 851) in their investigation of the constituents of the root bark of this tree. They confirmed the formula $C_{26}H_{28}O_{14}$ (with eight hydroxy-groups) for morindin, and they further showed that in all probability morindone was a trihydroxymethylanthraquinone derived from 2-methylanthraquinone, since, when distilled with zinc dust, 2-methylanthracene was obtained.

Subsequently, Oesterle and Tisza (*Arch. Pharm.*, 1907, **245**, 534) investigated once more the constituents of *M. citrifolia*. They drew the conclusion that morindin from that source had the formula $C_{27}H_{30}O_{15}$ and contained nine hydroxy-groups. They based this conclusion on an analysis of morindin, its acetyl and benzoyl derivatives, and on a quantitative determination of the products of hydrolysis. The properties of the morindin obtained by these authors, and also those of its derivatives, are at distinct

variance with those described by Perkin and Hummel (*loc. cit.*). Perkin (P., 1908, **24**, 150) directed attention to these discrepancies and published further analyses in support of his formula for morindin from *M. umbellata*, and suggested that the morindin derived from *M. umbellata* and *M. citrifolia* might be different.

With regard to the constitution of morindone, beyond the fact that it possesses the formula $C_{15}H_{10}O_5$, contains three hydroxy-groups, and yields 2-methylanthracene on distillation with zinc dust, little is known. Perkin (Thorpe's 'Dictionary of Applied Chemistry,' III, 547) has suggested either that morindone might be a methylanthragallol or that it might contain a $\cdot CH_2 \cdot OH$ group, the presence of such a group having been suggested by Robinson and Simonsen (T., 1909, **95**, 1088) to explain the relationship between aloë-emodin and rhein, since, as he pointed out, the colour reactions of morindone are somewhat remarkable.

For the preparation of the morindin and morindone required for the experiments described in this paper, the author has used the root bark of *M. citrifolia*, which was obtained for him by Dr. J. R. Henderson, of the Madras Museum, and Mr. Y. Narasihman, lecturer in chemistry, Maharaja's College, Vizianagram, and a considerable quantity of the bark was very kindly extracted for him by Drs. Fowler and Watson at the Indian Institute of Science, Bangalore. The author wishes to take this opportunity of expressing his thanks to these gentlemen.

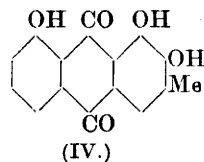
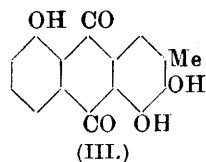
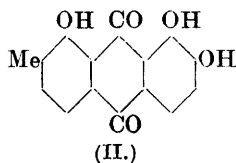
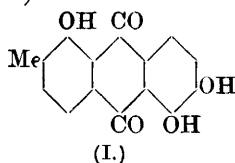
The morindin was extracted and purified essentially by the methods used by Perkin and Hummel, and it is not necessary to describe them in detail. In view of the discrepancies between the work of Perkin and Hummel and that of Oesterle and Tisza mentioned above, a specimen of morindin was very carefully purified by repeated crystallisation from 75 per cent. alcohol, when it was obtained in voluminous, yellow needles which, when rapidly heated, melted at 250—251°; when slowly heated, it sintered at 235° and melted at 245°. (Oesterle and Tisza state that it commenced to sublime at 235° and melted at 245°. Perkin and Hummel do not give a melting point.) The analytical data agreed well with the formula $C_{26}H_{28}O_{14}$ suggested by Perkin. The acetyl derivative was also prepared, and was found to melt at 239—240°. (Oesterle and Tisza give 236°, Perkin 246—248°.) As stated by Perkin, it is very sparingly soluble in cold alcohol, somewhat more readily so in the hot solvent, and contains eight acetyl groups. There would therefore appear to be no difference between the morindin derived from *M. citrifolia* and *M. umbellata*, and the discrepancies between the results of Perkin and Hummel and those of Oesterle and Tisza must be ascribed to some other cause. The author had

hoped to make a direct comparison of the morindins obtained from these two sources, but up to the present he has not succeeded in obtaining a specimen of the root bark of *M. umbellata*.

Attempts to isolate in a pure state the sugar formed by the hydrolysis of morindin were unsuccessful. The phenylosazone was prepared, but was found to be a mixture.

The Constitution of Morindone.

From a consideration of the experiments described in this paper and from the results obtained by previous investigators, the author would suggest that morindone is best represented either as a hydroxymethylanthrarufin (I) or as a hydroxymethylchryszazin (II).



The evidence in support of this view may, perhaps, best be summarised as follows:

(i) The methyl group is in position 2, since morindone on distillation with zinc dust yielded 2-methylantracene (Perkin and Hummel, *loc. cit.*, p. 856).

(ii) Morindone contains three hydroxy-groups, since it yields triacetyl, tribenzoyl, and trimethoxy-derivatives.

(iii) Two of the hydroxy-groups must be in the ortho-position with respect to the carbonyl groups of the anthraquinone nucleus, since treatment with methyl iodide and alkali only yielded a monomethyl ether (see p. 773).

(iv) Morindone is a mordant dye resembling alizarin, and hence probably has two of the hydroxy-groups in the 1:2-position.

(v) The hydroxy-group, which undergoes methylation with methyl iodide, must be present in the same ring as another hydroxy-group, since *morindone monomethyl ether* is completely destroyed when oxidised with an alkaline solution of potassium permanganate, only oxalic acid being isolated from the products (see p. 773).

(vi) Morindone cannot be a derivative of anthragallol or purpurin, since it is perfectly stable in alkaline solution and does not undergo oxidation even when air is drawn through such a solution for several days.

(vii) The presence of a $\cdot\text{CH}_2\cdot\text{OH}$ group, as suggested by Perkin, is unlikely, since all attempts to detect such an alcoholic grouping by oxidation or displacement of the hydroxy-group by a halogen were unsuccessful.

From the above, it follows that the only positions for the hydroxy-groups are as in 1:5:6-trihydroxyanthraquinone or 1:7:8-trihydroxyanthraquinone.

(viii) It is suggested that the methyl group must be in the ortho-position with respect to one of the hydroxy-groups, since all attempts to oxidise it to a carboxyl group by means of chromic acid have proved unsuccessful, the molecule being completely destroyed when once attacked by the oxidising agent. As is well known, *o*-xylene cannot be oxidised to phthalic acid by means of chromic acid, and the author has further found that whereas *p*-tolyl methyl ether when oxidised by means of chromic acid in acetic acid solution gave an excellent yield of anisic acid, *o*-tolyl methyl ether under similar conditions did not yield a trace of the corresponding *o*-methoxy-acid.

(ix) If the view be accepted that the methyl group is in the ortho-position with respect to one of the hydroxy-groups, then four formulæ derived from hydroxyanthrarufin or hydroxychryszazin become possible (I, II, III, and IV). The author would reject formulæ III and IV, since it is highly improbable that substances possessing these formulæ would be methylated by methyl iodide, owing to steric hindrance.

(x) In deciding between formulæ I and II, it would appear that formula I is the more probable, since in its colour reactions morindone resembles more closely hydroxyanthrarufin than hydroxychryszazin. Hydroxyanthrarufin dissolves in sulphuric acid with a violet colour which, on the addition of boric acid, becomes blue; morindone dissolves in sulphuric acid with a blue colour, which is not changed on the addition of boric acid; moreover, the sulphuric-boric acid solutions of hydroxyanthrarufin and morindone are practically indistinguishable in colour. Hydroxychryszazin, on the other hand, dissolves in sulphuric acid with a red colour, which becomes purple on the addition of boric acid. The bluer shades exhibited by morindone are explained by the presence of the methyl group, since, as is well known, methylalizarin yields bluer shades than does alizarin.

Many experiments were made with the object of confirming the

formula suggested above for morindone, but up to the present without success. Morindone trimethyl ether was found to be extremely resistant to oxidising agents. It was only slowly attacked by an alkaline solution of potassium permanganate even in boiling solution. Experiments involving the use of either chromic acid or nitric acid gave only negative results.

The synthesis of morindone is being attempted, but the problem seems to be a difficult one.

EXPERIMENTAL.

Morindin.

The material, isolated and crystallised as described on p. 767 (Found: C=55.3; H=4.9. $C_{26}H_{28}O_{14}$ requires C=55.3; H=4.9 per cent.), was hydrolysed with an alcoholic solution of sulphuric acid, when 0.7556 gave 0.3632 morindone. Yield of morindone=48.1 per cent., whereas if the formula for morindin were $C_{26}H_{28}O_{14}$, the yield of morindone should be 48.0 per cent.

Acetylmorindin.—This substance was readily prepared by boiling morindin with acetic anhydride containing a trace of pyridine for two hours. It separated from dilute acetic acid in pale sulphur-yellow needles, which melted at 239—240°. For analysis it was dried at 120° (Found: C=56.1; H=5.1. $C_{42}H_{44}O_{22}$ requires C=56.0; H=4.9 per cent.). The number of acetyl groups present was determined by A. G. Perkin's method, and was found to be eight. 0.2074 gave 0.1103 $C_2H_4O_2$, whence Ac=38.2, whereas this amount of a substance of the formula $C_{26}H_{20}O_{14}(Ac)_8$ should yield 0.1106 $C_2H_4O_2$, Ac=38.2 per cent.*

Morindone.

The morindone required for these experiments was obtained from morindin by hydrolysis with an alcoholic solution of sulphuric acid. After crystallisation from toluene, it melted at 275°, and showed all the properties ascribed to this substance (Found: C=66.4; H=3.7. Calc.: C=66.7; H=3.7 per cent.). Morindone was not attacked when heated with an acetic acid solution of hydrogen bromide (saturated at 0°) for some hours at 100° in a sealed tube, nor was it found to be altered when air was drawn through an alkaline solution for some days.

Acetylmorindone.—Acetylmorindone was prepared by heating morindone for two hours with acetic anhydride and anhydrous

* Oesterle and Tisza's formula $C_{27}H_{21}O_{18}(Ac)_9$ requires Ac=39.8 per cent.

sodium acetate. It was purified by crystallisation from acetic acid, when it was obtained in pale yellow needles melting at 249° and commencing to sinter slightly at 243° . This melting point is considerably higher than that given by Perkin and Hummel (*loc. cit.*, p. 856), who state that acetylmorindone melts at 222° . I am, however, informed by Prof. Perkin that this value for the melting point is probably due to a misprint.

For analysis, a specimen was dried at 120° :

0.1129 gave 0.2645 CO_2 and 0.0427 H_2O . C = 63.8; H = 4.2.

$\text{C}_{21}\text{H}_{16}\text{O}_8$ requires C = 63.6; H = 4.0 per cent.

Acetylmorindone was not readily attacked by chromic acid, and all attempts to oxidise the methyl group by this reagent were unsuccessful. Thus, when treated with the quantity of chromic acid calculated to oxidise the methyl group to a carboxyl group, a portion of the substance appeared to undergo complete destruction, the remainder being unattacked. A careful examination of the chromic acid solution failed to reveal the presence of any derivative of phthalic acid. When treated with an acetic acid solution of hydrogen bromide (saturated at 0°) in a sealed tube at 100° , hydrolysis of the acetyl derivative took place, but no trace of a halogen derivative was formed, as would in all probability have been the case if a $\cdot\text{CH}_2\cdot\text{OAc}$ group had been present (compare Perkin and Simonsen, T., 1904, **85**, 854; Müller, T., 1907, **91**, 1782).

Benzoylmorindone.—Morindone (1 gram) was mixed with pyridine (5 c.c.), and, after cooling in ice, benzoyl chloride (2 grams) was gradually added. The reaction proceeded readily, and, after remaining for thirty minutes, the mixture was poured into water, when a viscid oil separated, which rapidly solidified on triturating with hot alcohol. It was crystallised from acetic acid, when it was obtained in nodules of fine, yellow needles melting at 218 — 219° . For analysis, it was dried at 120° :

0.1079 gave 0.2924 CO_2 and 0.0403 H_2O . C = 73.9; H = 4.1.

$\text{C}_{36}\text{H}_{22}\text{O}_8$ requires C = 74.2; H = 3.8 per cent.

Methylation of Morindone: Morindone Monomethyl Ether and Trimethyl Ether.

Many experiments were made with a view to devise a satisfactory method for the preparation of morindone trimethyl ether. It was ultimately found that the following somewhat laborious process gave the best results.

Morindone (3 grams) was mixed with a solution of potassium

hydroxide (12 grams) dissolved in water (15 c.c.) and treated with methyl sulphate (15 c.c.), which was added all at once. The mixture was vigorously stirred, and when the reaction was complete, the same quantities of alkali and methyl sulphate were added. The alkaline solution, which was now deep red, was boiled, acidified, the crude methylation product collected, and again treated with alkali and methyl sulphate as before. The red solution contained in suspension a deep red, sparingly soluble potassium salt and the yellow trimethyl ether. It was filtered through cloth, and the residue boiled with dilute alkali and filtered, this treatment being repeated three times, when the filtrate should only be slightly red. The residue was ground with a considerable volume of chloroform, which dissolved the morindone trimethyl ether, leaving the insoluble, red potassium salt of the monomethyl ether *A* (see p. 773). The chloroform extract was evaporated, the crude, pale yellow trimethyl ether dissolved in hot toluene, and the toluene solution repeatedly washed with hot dilute alkali, which removed a further quantity of partly methylated morindone. (The alkaline washings were mixed with *A*.)

After separating from the alkali, the toluene solution was filtered, the toluene removed in a current of steam, when the nearly pure trimethyl ether was obtained. It was crystallised from acetic acid, when it separated in pale yellow needles melting at 229°, as stated by Oesterle and Tisza :

0.1013 gave 0.2566 CO₂ and 0.0426 H₂O. C=69.1; H=4.7.

C₁₈H₁₆O₅ requires C=69.2; H=5.1 per cent.

Morindone trimethyl ether, when pure, is insoluble in alkali; in sulphuric acid it dissolves to a deep blue solution.

The oxidation of morindone trimethyl ether has been carefully investigated. The ether was found to be extremely stable to chromic acid, and the greater part was recovered unchanged when oxidised with the equivalent quantity of oxidising agent, the remainder being apparently completely destroyed. When suspended in dilute sodium carbonate solution and boiled with a solution of potassium permanganate for several days, it was slowly oxidised. Much of the ether remained unattacked, and, with the exception of oxalic acid, no acid could be isolated in sufficient quantity for identification. When nitric acid was used as the oxidising agent, only oxalic acid appeared to be formed.

The sparingly soluble red potassium salt *A*, mentioned above, was suspended in hot water, decomposed with hydrochloric acid, and the brown solid which separated was collected. It was purified

by repeated crystallisation from acetic acid. For analysis, it was dried at 120°:

0.1012 gave 0.251 CO₂ and 0.0388 H₂O. C=67.6; H=4.2.

0.1028 ,, 0.2561 CO₂ ,, 0.038 H₂O. C=67.9; H=4.1.

C₁₆H₁₂O₅ requires C=67.6; H=4.2 per cent.

Morindone monomethyl ether crystallises in iridescent, brown needles melting at 248°. It is readily soluble in chloroform, toluene, or hot acetic acid, more sparingly so in ether or ethyl acetate, and very sparingly so in alcohol. It dissolves in concentrated sulphuric acid with a colour similar to that shown by morindone, only slightly redder. The sulphuric acid solution on the addition of a crystal of potassium nitrate gives a fine, greenish-red coloration. In fuming nitric acid, it dissolves with a transient red colour, yielding almost immediately a reddish-brown solution. It forms sparingly soluble red sodium and potassium salts, the solutions of which exhibited a slight fluorescence reminiscent of eosin. An attempt was made to determine the number of methoxy-groups present by the ordinary Zeisel method, but owing to the sparing solubility of the substance, the results were always low, although the heating was continued for from four to five hours and the hydriodic acid was mixed with acetic anhydride. *Morindone monomethyl ether* is readily attacked by an alkaline solution of potassium permanganate; it appears to undergo complete disintegration, and the bearing of this fact on the determination of the constitution of morindone has already been discussed.

Morindone monomethyl ether was also prepared by treating morindone with methyl iodide in the presence of sodium methoxide. Morindone (0.5 gram) was mixed with sodium methoxide (1.3 grams of sodium), and, after the addition of methyl iodide (0.8 gram), the mixture was heated in a sealed tube at 100° for eight hours. The deeply coloured product was poured into water, and, after the addition of potassium hydroxide solution, was boiled, filtered, and the residual potassium salt well washed with hot dilute alkali until the washings were only faintly coloured. The salt was decomposed with dilute hydrochloric acid, and the brown solid thus obtained (0.1 gram) was collected and recrystallised from acetic acid, when it melted at 247—248° and showed all the properties of morindone monomethyl ether. The melting point was not altered on admixture with an equal amount of the monomethyl ether prepared by means of methyl sulphate, as described above.

Diacetylmorindone Monomethyl Ether.—This substance was

readily prepared when the monomethyl ether was heated for two hours with acetic anhydride and anhydrous sodium acetate. It was crystallised from acetic acid and dried at 120° for analysis:

0.1042 gave 0.2494 CO_2 and 0.041 H_2O . C=65.3; H=4.3.

$\text{C}_{20}\text{H}_{15}\text{O}_7$ requires C=65.2; H=4.3 per cent.

Diacetylmorindone monomethyl ether separates from acetic acid in yellow, hexagonal prisms melting at $245\text{--}246^{\circ}$. It is sparingly soluble in hot alcohol.

The Sugars from Morindin.

In one experiment, the acid mother liquor from which the morindone had been separated was treated with sodium acetate until the excess of mineral acid was neutralised, and the solution concentrated to a small bulk. Excess of phenylhydrazine was added, and, after heating on the water-bath for one hour, the brownish-yellow osazone was collected. After repeated fractional crystallisation from alcohol, a sparingly soluble fraction was obtained which separated in fine yellow needles decomposing at 207° :

0.0689 gave 11 c.c. N_2 at 30° and 760 mm. N=17.2.

$\text{C}_{17}\text{H}_{20}\text{O}_3\text{N}_4$ requires N=17.1 per cent.

This substance would, therefore, appear to be the osazone of a pentose, and is possibly identical with the osazone (m. p. $202\text{--}203^{\circ}$) described by Perkin (*loc. cit.*, p. 150), but owing to the small quantity of material which was obtained in a pure state, great trust cannot be placed in the result of the analysis. From the mother liquor from which the above-mentioned osazone had been separated, a small quantity of another osazone was isolated, in stout yellow needles, which melted at about 195° and were readily soluble in alcohol.

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