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CCLXXXVIII.—*The Constitution and Synthesis of Embelic Acid (Embelin), the Active Principle of* Embelia Ribes.

By K. HABIB HASAN and EDGAR STEDMAN.

THE berries of *Embelia Ribes* are used extensively in India on account of their anthelmintic properties. The active principle, embelic acid, to which these properties are due, and also its ammonium salt have been introduced into Europe, but have probably never been utilised to any great extent. The first chemical investigation of the berries appears to be that of Scott (*Chemist and Druggist*, 1888; quoted by Heffter and Feuerstein, see below), who isolated from them a substance which crystallised in the form of bright

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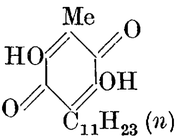
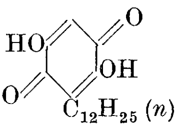
yellow scales. Scott regarded this substance as a glucoside and proposed the name " embelin " for it. Shortly afterwards, Warden (*Pharm. J.*, 1888, **18**, 601; **19**, 305) examined the berries and isolated a substance, probably identical with the so-called glucoside of Scott, to which he assigned the formula $C_9H_{14}O_2$. In view of the definite acidic properties of the compound, as shown, for example, by the formation of a crystalline ammonium salt, Warden proposed the name " embelic acid " for it.

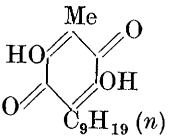
No further work appears to have been done on this subject until Heffter and Feuerstein (*Arch. Pharm.*, 1900, **238**, 15) submitted embelic acid to a detailed chemical investigation. These authors confirmed both the acidic properties of the substance and the analytical results, but they provided evidence which necessitated revising the molecular formula to $C_{18}H_{28}O_4$. They were further able to show that two of the oxygen atoms were present as hydroxyl groups, since embelic acid formed a dibenzoyl derivative, and that these groups were responsible for its acidic properties. The remaining oxygen atoms could be readily reduced with the formation of dihydroembelic acid, a colourless substance which underwent spontaneous oxidation in the air to the orange-coloured embelic acid. In view of the latter behaviour, coupled with the fact that embelic acid condensed readily with primary amines, such as methylamine, aniline, and toluidine, Heffter and Feuerstein concluded that the substance was a *p*-quinone. The same authors submitted embelic acid to oxidation, and isolated from the product an acid, which they identified as lauric acid, together with smaller amounts of simpler acids. On the basis of these results, they proposed formula (I) for embelic acid, although they pointed out the possibility of a different orientation of the substituent groups.



(I.)



(II.)



(III.)

In devising the above formula, Heffter and Feuerstein made the tacit assumption that the lauric acid formed by oxidation of embelic acid was derived from the large side chain together with one carbon atom from the ring, and it was this assumption which necessitated the introduction of the methyl group shown in their formula, although no positive evidence for the existence of this group was obtained experimentally. They apparently overlooked the possibility that the lauric acid might originate entirely from the side

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chain, in which case the constitution of embelic acid would be represented by (II).

Since degradation experiments were unlikely to lead to results which would permit of a decision between these formulæ, it was decided to synthesise both compounds. It was first necessary, however, in view of the recent work of Kaul, Ray, and Dutt (*J. Indian Chem. Soc.*, 1929, **6**, 577), to repeat the oxidation of embelic acid. These authors, who have reintroduced the name embelin for the compound under consideration, have prepared a number of derivatives of embelic acid, the formation of which gives general support to Heffter and Feuerstein's formula. They claim, however, that the acid produced on oxidation is not lauric acid, but an isomeride which they describe as *iso*lauric acid. We have therefore repeated this oxidation, using two methods. In the first, the oxidation was effected with alkaline permanganate under exactly the same conditions as those employed by Heffter and Feuerstein. The acid so obtained was distilled under diminished pressure, and then melted at about 32°, *i.e.*, about 10° lower than lauric acid. Nevertheless, when converted into its amide by successive treatment with thionyl chloride and ammonia, a product was obtained which, after crystallisation from ligroin, melted at 96°, and proved to be identical with a specimen of the amide similarly prepared from some lauric acid supplied by the British Drug Houses Ltd. In the second method, nitric acid was employed as oxidising agent under the conditions described by Kaul, Ray, and Dutt. After distillation, the acid again proved to be impure, but by conversion into its sodium salt and regeneration from the latter after thorough washing with water, it melted at 42°, and the m. p. showed no depression when it was admixed with an approximately equal amount of the above-mentioned lauric acid.

In view of this result, it was decided to proceed, in the first instance, with the synthesis of the substance represented by formula (I). Owing, however, to the difficulty in procuring the large quantities of undecoic acid required for this synthesis, a lower homologue, 2 : 5-*dihydroxy*-4-n-*nonyl*-p-*toluquinone* (III), was first prepared in order to gain information regarding the properties of the intermediate compounds and the conditions under which the various reactions took place. In this synthesis, the easily procurable pelargonic acid could be utilised.

Toluene was condensed with nonoyl chloride in the presence of aluminium chloride to give p-*tolyl* n-*octyl* *ketone* (IV), which on reduction by Clemmensen's method yielded 4-n-*nonyltoluene* (V). Nitration of the latter gave a mixture of 2- and 3-nitro-4-*n*-nonyltoluenes (VI and VII), which was reduced, without separation of the

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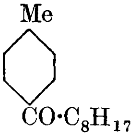
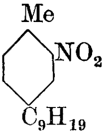
isomerides, with iron powder and acetic acid to the corresponding amines. Since both amines should yield, on oxidation, the same quinone (VIII), which was the next step in the projected synthesis, it was unnecessary to separate the isomerides. Nevertheless, pure specimens of the normal *sulphates* were actually obtained by fractional crystallisation of this salt. The conversion of 4-n-*nonyl*-p-*toluquinone* (VIII), obtained by oxidation of the amines with sodium dichromate and sulphuric acid, into the required 2 : 5-dihydroxy-4-*n*-nonyltoluquinone (III) was effected by the method developed by Zincke (*Ber.*, 1885, **18**, 787), Kehrmann (*Ber.*, 1891, **23**, 897), and Fichter (*Ber.*, 1904, **37**, 2388; *Annalen*, 1908, **361**, 363) for the conversion of *p*-quinones into dihydroxyquinones. An alcoholic solution of the quinone was treated with excess of an alcoholic solution of methylamine, and 2 : 5-*di*(*methylamino*)-4-n-*nonyl*-p-*toluquinone* (IX) separated. Corresponding with the theory, according to which this reaction takes the following course: $3C_9H_{19}\cdot C_6H_2MeO_2 + 2NH_2Me = C_9H_{19}\cdot C_6MeO_2(NHMe)_2 + 2C_9H_{19}\cdot C_6MeH_2(OH)_2$, the yield of this substance amounted to *ca.* 30% of the quinone used. Hydrolysis of the dimethylamino-compound with 40% sulphuric acid yielded 2 : 5-dihydroxy-4-*n*-nonyl-*p*-toluquinone (III). This substance exhibited properties similar to those of embelic acid. It crystallised in lustrous deep orange plates, and gave a violet coloration with alkalis due to the formation of coloured salts.



(IV.)

(V.)



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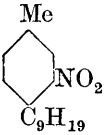
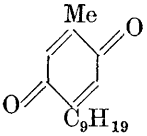
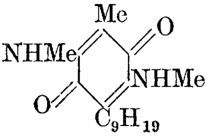


(VII.)



(VIII.)



(IX.)

By using a series of reactions identical with those outlined above, but starting from toluene and undecoyl chloride, 2 : 5-*dihydroxy*-4-n-*undecyl*-p-*toluquinone* (I) was synthesised. All the reactions proceeded similarly, but some difficulty was at first experienced in hydrolysing the di(methylamino)-compound. This could not be effected with 40% aqueous sulphuric acid, but took place smoothly on increasing the concentration of the acid to 70% and adding

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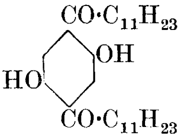
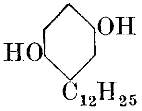
alcohol. The 2 : 5-dihydroxy-4-*n*-undecyl-*p*-toluquinone thus obtained resembled natural embelic acid closely in properties, but the synthetic material had a somewhat redder shade and melted at 150°, *i.e.*, 7° higher than the natural substance. Moreover, a mixture of approximately equal quantities of the two compounds melted at about 125°. It is thus clear that embelic acid is not 2 : 5-dihydroxy-4-*n*-undecyl-*p*-toluquinone.

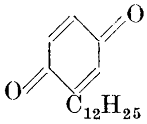
Having thus definitely shown that Heffter and Feuerstein's formula for embelic acid was incorrect, the synthesis of the substance corresponding with the alternative formula (II) was carried out. Quinol was condensed by Nencki's method (*J. pr. Chem.*, 1881, **23**, 546) with lauric acid. The reaction did not take the course normally followed, according to the literature, with acids of smaller molecular weight, for, in place of the expected lauroylquinol, *dilauroylquinol* (probably X) was obtained. Nevertheless, on reduction by Clemmensen's method, simultaneous hydrolysis and reduction occurred, and the required *laurylquinol* (XI) was isolated from the reaction mixture. Large quantities of quinol and lauric acid were also present; it is evident from this, as well as from the small yield of laurylquinol, that hydrolysis was not restricted to one lauroyl group. Oxidation of laurylquinol with sodium dichromate and sulphuric acid gave *lauryl*-p-*benzoquinone* (XII), which reacted with methylamine under the conditions outlined above to give 2 : 5-*di*(*methylamino*)-3-*lauryl*-p-*benzoquinone* (XIII). On hydrolysis with sulphuric acid in the presence of alcohol, this yielded 2 : 5-*dihydroxy*-3-*lauryl*-p-*benzoquinone* (II), which proved to be identical with natural embelic acid. Like the latter, it melted at 143°, and no depression occurred when the two substances were admixed. Further confirmation was afforded by the identity of the tetra-acetyl derivatives prepared from the natural and the synthetic compound by reductive acetylation, and of the dibenzoyl derivatives. Embelic acid is thus 2 : 5-dihydroxy-3-lauryl-*p*-benzoquinone (II).



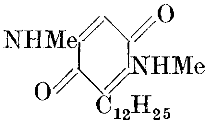
(X.)



(XI.)



(XII.)



(XIII.)

The elucidation of the structure of this acid opens up the possibility of studying the relationship between the constitution of this compound and its anthelmintic properties. With this object, as well as with a view to the synthesis of new anthelmintics, one of us proposes to prepare and test for anthelmintic properties a number

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of analogous and related compounds, particularly of the quinone and hydroxyquinone type.

EXPERIMENTAL.

Isolation of Embelic Acid.—The dried berries of *Embelia Ribes* were crushed and extracted continuously with ether. The tarry residue which remained on evaporation of the solvent was dissolved in rectified spirit, and yellowish-red material then slowly separated. This was recrystallised first from alcohol and then from chloroform, the embelic acid being obtained in the form of orange-red plates, m. p. 143°. This appeared to be quite pure, but was found to be of a redder tinge than the synthetic material subsequently obtained. A further examination of the natural substance then showed that it was contaminated with a minute amount of impurity which was responsible for the deeper colour and could only be removed with difficulty. By dissolving the embelic acid in hot alcohol and allowing it to crystallise out slowly, it was found that the first crystals which were deposited were of a deep red colour. Apparently these had adsorbed the impurity, for, on decantation of the mother-liquor, orange crystals separated. After several repetitions of this process, the natural material was obtained in the form of orange plates, identical in colour with the synthetic substance. Separation from the red impurity was also effected by sublimation under diminished pressure and subsequent crystallisation.

p-*Tolyl* n-*Octyl Ketone* (IV).—To a mixture of nonoyl chloride (177 g.) and toluene (105 g.), aluminium chloride (290 g.) was added. After the initial vigorous reaction had subsided, the mixture was heated on the water-bath for 2—3 hours. Water was then cautiously added to the cold mixture, and the product separated as an oily layer which solidified on cooling. This was extracted with ether, the extract washed successively with water, sodium hydroxide, and water, and then dried over potassium carbonate. The residue from the evaporation of the ether was distilled under diminished pressure and the fraction passing over between 185° and 190°/15 mm. collected separately; yield, 186 g. p-*Tolyl* n-*octyl ketone* boils at 183—184°/12 mm. and solidifies, on cooling, to a mass of colourless waxy crystals, m. p. 37° (Found: C, 82·5; H, 10·2. $C_{16}H_{24}O$ requires C, 82·8; H, 10·3%). It possesses a characteristic odour slightly reminiscent of that of bitter almonds.

4-n-*Nonyltoluene* (V).—The above ketone (100 g.) was mixed with 400—500 g. of amalgamated zinc wool and 50 c.c. of 15% hydrochloric acid. The mixture was then boiled vigorously under reflux for 6—7 hours, further quantities of acid being added occasionally, bringing the total volume up to 400—500 c.c. The product was

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extracted with ether, the extracts washed, and dried over potassium carbonate. The residue from the evaporation of the ether boiled between 155° and 170°/12 mm., the fraction passing over at 160—162°/12 mm., which constituted the bulk of the material, being collected separately. On redistillation this yielded 4-n-*nonyltoluene*, a colourless liquid, b. p. 160—161°/12 mm. (Found : C, 87·7 ; H, 11·9. $C_{16}H_{26}$ requires C, 88·1 ; H, 11·9%), which does not solidify when cooled in a freezing mixture; yield, 70 g. It possesses an odour similar to that of the ketone.

Nitration of 4-n-*Nonyltoluene.*—This nitration was first attempted at 0°, but the hydrocarbon was practically unattacked at this temperature. After a number of experiments under different conditions the following procedure was finally adopted : a cold mixture of 10 g. of concentrated nitric acid with 20 g. of concentrated sulphuric acid was added slowly to 10 g. of the hydrocarbon, which was stirred vigorously and maintained at 15°. After the addition of the nitrating mixture, the stirring was continued for one hour, during which the temperature was allowed to rise to 20°. The mixture was then poured into water, and the product extracted with ether. The ethereal extract was washed repeatedly with dilute sodium hydroxide, until all free acid had been removed, and finally with water. After drying over potassium carbonate and evaporation of the ether, a dark brown residue was obtained. This was fractionally distilled under diminished pressure. At 160°/12 mm., a small amount of unchanged hydrocarbon was collected. The temperature then rapidly rose, the bulk of the material distilling at 190—200°/12 mm. On redistilling this fraction, a mixture of 2- and 3-nitro-4-*n*-nonyltoluene (VI and VII), a thick yellow liquid with an odour similar to but more intense than that of the preceding compounds, b. p. 198—200°/12 mm., was obtained (Found : C, 72·9; H, 9·3; N, 5·2. Calc. for $C_{16}H_{25}O_2N$: C, 73·0; H, 9·5; N, 5·3%).

Reduction of above Nitro-compounds.—To a mixture of the nitro-compounds (10 g.) with reduced iron powder (12 g.) contained in a flask fitted with a stirrer and reflux condenser, 10 c.c. of 50% acetic acid were added, and the whole was warmed on the water-bath, with stirring ; a vigorous reaction commenced, and heating was then discontinued. After the abatement of this reaction, further quantities of the acid solution were added at intervals, a total volume of 100 c.c. being used, and the mixture was continuously stirred and maintained in active ebullition for 3 hours. The cold mixture was then filtered at the pump. On account of their high hydrocarbon content, the salts of the resulting amines possessed unusual properties : they were insoluble in water and soluble in moist ether. As a result, the bulk of the product was contained in the above solid

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residue. Both the latter and the filtrate were therefore extracted separately with ether, and the acetate contained in the combined extracts was decomposed by shaking the latter with strong aqueous sodium hydroxide. The ethereal solution was separated, washed with water, and dried over potassium carbonate, and the residue obtained on removal of the ether was distilled under diminished pressure. A mixture of the two amines was thus obtained in 90% yield as a colourless oil, b. p. 180—190°/12 mm. The direct separation of the isomeric amines was not attempted, but two pure sulphates were isolated. The above mixture of amines was poured into an excess of dilute sulphuric acid, and a pasty mass of the mixed sulphates at once separated. The liquid was removed by decantation, and the residue washed repeatedly with water, becoming granular. It was then filtered, and dried in a desiccator. Partial separation of the *sulphates* of 2- and 3-amino-4-*n*-nonyltoluene was originally effected by grinding the solid with dry ether, but it was subsequently found preferable to crystallise the mixture fractionally from acetone. The less soluble fraction, after two recrystallisations from alcohol, formed plates, m. p. 178° (Found: C, 67·9; H, 9·8; N, 4·8; S, 5·7. $C_{16}H_{27}N,\frac{1}{2}H_2SO_4$ requires C, 68·1; H, 9·9; N, 5·0; S, 5·7%). The more soluble fraction, after repeated crystallisation from alcohol, formed needles, m. p. 144° (Found: C, 68·0; H, 9·8; N, 5·0; S, 5·8%).

4-n-*Nonyl*-p-*toluquinone* (VIII).—A mixture of the finely ground sulphates (2 g.) obtained from the preceding reaction was suspended in a mixture of 16 c.c. of concentrated sulphuric acid with 60 c.c. of water and cooled to 10°. A solution of 0·75 g. of sodium dichromate in 10 c.c. of water was then added drop by drop with stirring. The colour changed through violet to black, and the solid became sticky. Stirring was continued for 2 hours, and the mixture then left overnight in the refrigerator. A further solution of 1·5 g. of sodium dichromate in 20 c.c. of water was then added under the same conditions. After 24 hours the quinone was extracted with ether, and the extract was washed with water and dried over calcium chloride. The residue from the ether was taken up in hot alcohol and filtered from some insoluble material, whereupon reddish-yellow plates separated from the filtrate. When recrystallised from alcohol, 4-n-*nonyl*-p-*toluquinone* forms yellow plates, m. p. 53° (Found: C, 77·3; H, 9·6. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%). The low yield (0·28 g.; 17%) could not be improved by varying the conditions. The difficulties encountered in the preparation of this quinone are attributable to the virtual insolubility of the sulphate of the amine in water.

2 : 5-*Di*(*methylamino*)-4-n-*nonyl*-p-*toluquinone* (IX).—A solution

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of 0·2 g. of the above quinone in alcohol was mixed with excess of a 33% alcoholic solution of methylamine. A violet-red precipitate separated. This was filtered off and crystallised from alcohol, in which it is only sparingly soluble. 2 : 5-*Di*(*methylamino*)-4-n-*nonyl*-p-*toluquinone* forms violet microscopic needles, m. p. 167° (Found : N, 7·6. $C_{18}H_{30}O_2N_2$ requires N, 7·9%).

2 : 5-*Dihydroxy*-4-n-*nonyl*-p-*toluquinone* (III).—A suspension of the preceding compound in 40% sulphuric acid was refluxed for one hour. The yellow solid thus produced was filtered off and crystallised from alcohol, the *toluquinone* being obtained as lustrous orange plates, m. p. 154° (Found : C, 68·7; H, 8·6. $C_{16}H_{24}O_4$ requires C, 68·6; H, 8·6%), in theoretical yield.

p-*Tolyl* n-*decyl ketone*, $CH_3{\cdot}C_6H_4{\cdot}CO{\cdot}C_{10}H_{21}$, b. p. 196—197°, m. p. 32° (Found : C, 82·8; H, 10·8. $C_{18}H_{28}O$ requires C, 83·1; H, 10·8%), was obtained in 80% yield from toluene and undecoyl chloride. The undecoic acid, from which the required undecoyl chloride was prepared, was obtained by the catalytic reduction of ethyl undecenoate; we are indebted to Professor T. P. Hilditch for carrying out this process for us.

4-n-*Undecyltoluene*, b. p. 171—172°/12 mm. (Found : C, 87·3; H, 11·8. $C_{18}H_{30}$ requires C, 87·8; H, 12·2%), was isolated in 73% yield from the product of the Clemmensen reduction of the above ketone.

Nitration of 4-n-*Undecyltoluene*.—This was effected under exactly the same conditions as those used for the nitration of the corresponding nonyl compound. A mixture of 2- and 3-nitro-4-*n*-undecyltoluenes, b. p. 215—216°/12 mm. (Found : C, 74·0; H, 9·8; N, 4·8. Calc. for $C_{18}H_{29}O_2N$: C, 74·2; H, 10·0; N, 4·8%), was obtained in 72% yield.

Reduction of above Nitro-compounds.—Reduced iron powder and acetic acid were again employed for the reduction. The mixed amines were isolated in 80% yield as an oily liquid, b. p. 198—200°/12 mm. The sulphates were prepared, but it was not, in this case, found possible to separate the isomerides completely. The mixture of sulphates could be crystallised from acetone. The less soluble fraction, when repeatedly crystallised from alcohol, yielded what appeared to be a homogeneous *sulphate* in the form of colourless leaflets, m. p. 177° (Found : S, 5·2. $C_{18}H_{31}N,\frac{1}{2}H_2SO_4$ requires S, 5·2%).

4-n-*Undecyl*-p-*toluquinone*, $CH_3{\cdot}C_6H_2O_2{\cdot}C_{11}H_{23}$, which crystallises from alcohol in lustrous yellow plates, m. p. 64° (Found : C, 78·2; H, 9·8. $C_{18}H_{28}O_2$ requires C, 78·3; H, 10·1%), was obtained in 22% yield by the oxidation of the preceding amines. It was found advantageous to use a larger excess of sodium dichromate in the

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second stage of the oxidation than was employed in the preparation of the corresponding nonyl compound, and to keep the reaction mixture at room temperature for 2—3 days.

2 : 5-*Di*(*methylamino*)-4-n-*undecyl*-p-*toluquinone*,

$CH_3 \cdot C_6O_2(NHMe)_2 \cdot C_{11}H_{23}$,

crystallises from alcohol, in which it is sparingly soluble, in dark violet microscopic needles, m. p. 158° (Found : N, 8·1 : $C_{20}H_{34}O_2N_2$ requires N, 8·4%).

2 : 5-*Dihydroxy*-4-n-*undecyl*-p-*toluquinone*,

$CH_3 \cdot C_6O_2(OH)_2 \cdot C_{11}H_{23}$.

—The preceding methylamino-compound is not attacked by boiling 40% sulphuric acid. When refluxed, however, for about an hour with 80% sulphuric acid in the presence of alcohol, it is hydrolysed smoothly and quantitatively. When crystallised from chloroform, 2 : 5-*dihydroxy*-4-n-*undecyl*-p-*toluquinone* forms lustrous orange-red plates, m. p. 150° (Found : C, 70·1 ; H, 9·0. $C_{18}H_{28}O_4$ requires C, 70·1 ; H, 9·1%).

Dilauroylquinol (probably X).—Zinc chloride (68 g.) was dissolved in hot lauric acid (300 g.), and quinol (55 g.) was added gradually to the hot mass with vigorous shaking. The temperature of the reaction mixture was maintained at 130—140° during this addition and for 2 hours subsequently. When cool, the dark brown product was thoroughly extracted with water to remove unchanged quinol, and the excess of lauric acid neutralised by the addition of sodium carbonate. The product was then filtered, and the solid and filtrate extracted separately with ether. The united extracts were washed with water, causing the separation of a small quantity of zinc laurate, and dried over calcium chloride. The solid residue obtained on evaporation of the ether was somewhat dark, and was therefore dissolved in methyl alcohol; the solution was boiled with animal charcoal. *Dilauroylquinol* separated from the filtrate (yield 80 g.), and crystallised from methyl alcohol as an almost colourless solid, m. p. 68° (Found : C, 75·5; H, 10·4. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

Laurylquinol (XI).—Dilauroylquinol (40 g.) was mixed with 200 g. of amalgamated zinc, 15% hydrochloric acid (50 c.c.) added, and the mixture boiled briskly, with stirring, for 6—8 hours. Further quantities of hydrochloric acid were added during this period, a total volume of 450 c.c. being used. The product was extracted with ether. The residue from the washed and dried ethereal extract was first thoroughly washed with water to remove considerable quantities of quinol, which had been formed by the hydrolytic decomposition of the dilauroylquinol during the reduction process, and then treated with sodium carbonate to neutralise the lauric acid similarly pro-

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duced. The resulting semi-solid mass was extracted with ether, and 11 g. of a brown product then crystallised spontaneously. When crystallised from benzene, *laurylquinol* forms colourless plates, m. p. 109° (Found: C, 77·4; H, 10·6. $C_{18}H_{30}O_2$ requires C, 77·7; H, 10·8%).

Lauryl-p-*benzoquinone* (XII).—Laurylquinol (5 g.) was suspended in 50 c.c. of 30% sulphuric acid, and a solution of 2·5 g. of sodium dichromate in 20 c.c. of water added. On refluxing the mixture for 30 minutes, oxidation took place smoothly and quantitatively, and the resulting quinone, which solidified on cooling, was filtered off. When recrystallised from alcohol, *lauryl*-p-*benzoquinone* forms pale yellow plates, m. p. 81° (Found: C, 77·7; H, 10·1. $C_{18}H_{28}O_2$ requires C, 78·3; H, 10·1%).

2 : 5-*Di*(*methylamino*)-3-n-*lauryl*-p-*benzoquinone* (XIII).—The above quinone was treated with alcoholic methylamine under the conditions previously described. 2 : 5-*Di*(*methylamino*)-3-n-*lauryl*-p-*benzoquinone* crystallises from alcohol, in which it is sparingly soluble, in violet microscopic needles, m. p. 147° (Found: N, 8·4. $C_{20}H_{34}O_2N_2$ requires N, 8·4%).

2 : 5-*Dihydroxy*-3-n-*lauryl*-p-*benzoquinone* (II).—The preceding methylamino-compound offered greater resistance to hydrolysis than the analogous compounds described above. It (0·5 g.) was suspended in 50 c.c. of 80% sulphuric acid and boiled. Sufficient alcohol was then added to the hot suspension to produce a clear solution, which was refluxed for 3 hours. On cooling, a yellow solid, together with some darker decomposition product, separated. This was filtered, and recrystallised twice from alcohol and finally from chloroform, 2 : 5-*dihydroxy*-3-n-*lauryl*-p-*benzoquinone*, orange plates with a golden lustre, m. p. 143°, being obtained (Found: C, 69·8; H, 9·1. $C_{18}H_{28}O_4$ requires C, 70·1; H, 9·1%). This substance was found to be identical with natural embelic acid. Both compounds melted at 143°, and no depression was produced when equal quantities of the two were intimately mixed. The synthetic, like the natural, substance gave a violet coloration with sodium hydroxide in the presence of alcohol, due to the formation of a coloured sodium salt which is soluble in alcohol and water, but only sparingly soluble in the latter solvent in the presence of excess of sodium hydroxide. As additional confirmation of the identity of the two compounds, the tetra-acetyl and dibenzoyl derivatives were prepared and compared. The former of these derivatives had already been prepared by the reductive acetylation of embelic acid by Kaul, Ray, and Dutt (*loc. cit.*), who state that it melts at 124°. The compound similarly prepared from the above synthetic embelic acid was found, however, to melt at 121°, whilst that from the natural substance had m. p.

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116° (Found: C, 65·1; H, 7·6. Calc. for $C_{26}H_{38}O_8$: C, 65·3; H, 7·9%), and was not changed by repeated recrystallisation from alcohol. A mixture of the two substances melted at 118°. While this result gave satisfactory confirmation of the identity of the synthetic and the natural compound, the slight discrepancy between the m. p.'s of the two acetyl derivatives could not, at first, be explained. When, however, the natural material was subjected to the processes of purification described above, the following figures were obtained for the m. p.'s of the tetra-acetyl derivatives: natural, 121°; synthetic, 120°; mixture, 119°; the synthetic compound was a different preparation from that previously examined.

The dibenzoyl derivatives were prepared by benzoylation of natural and synthetic embelic acid in pyridine solution with benzoyl chloride according to the procedure of Heffter and Feuerstein (*loc. cit.*). Both substances, as well as an intimate mixture of the two, melted at 98°

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