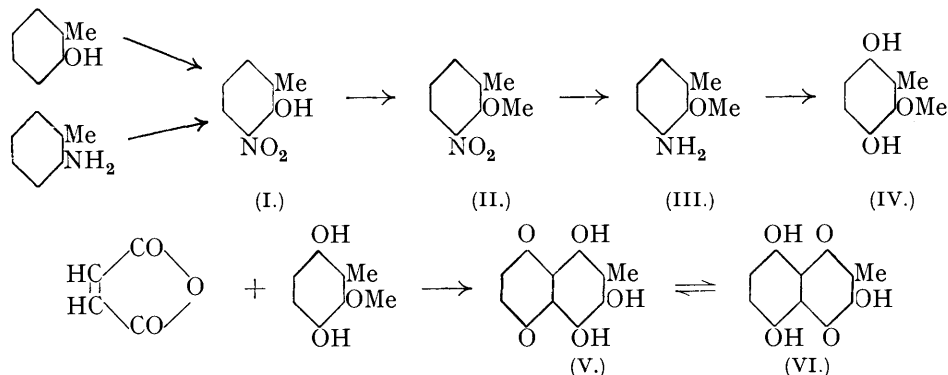


72. *The Colouring Matters of Drosera Whittakeri. Part III.*
The Synthesis of Hydroxydroserone.

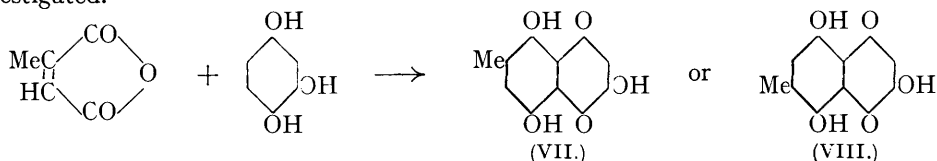
By F. L. WINZOR.

IN the two preceding papers it has been shown that droserone is probably 3 : 5 (or 3 : 8)-dihydroxy-2-methyl-1 : 4-naphthaquinone, and hydroxydroserone the 3 : 5 : 8-trihydroxy-2-methyl compound. The methods involved, however, do not provide absolute proof, and since oxalic and acetic acids were the only isolable products on oxidation, and methyl-naphthalene was not obtained in the degradation experiments carried out, it is desirable to establish the structures of the colouring matters by synthesis: this has now been achieved in the case of hydroxydroserone. The condensation of maleic anhydride with a suitable phenolic substance—successfully applied by Zahn and Ochwat (*Annalen*, 1928, 462, 51) in the synthesis of naphthazarin, and by Macbeth, Price, and Winzor (this vol., p. 333)—appeared to be the most promising line of attack. The obvious starting material,

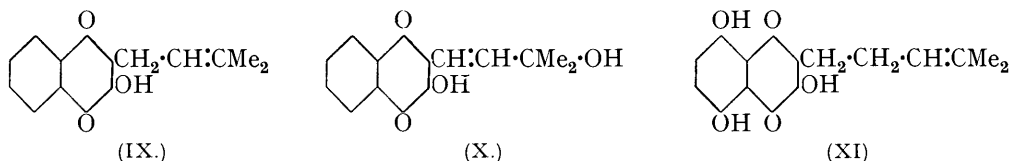
2 : 3 : 6-trihydroxytoluene, is not available, since toluquinone on treatment with acetic anhydride and sulphuric acid yields 2 : 4 : 5-triacetoxytoluene. 3 : 6-Dihydroxy-2-methoxytoluene (IV) is, however, available by the following series of reactions, and when condensed with maleic anhydride gives a product identical with hydroxydroserone.



The structure is further supported by the synthesis of the isomeric quinone with the methyl group in the other nucleus, 3 : 5 : 8-trihydroxy-6 (or 7)-methyl-1 : 4-naphthaquinone (VII, VIII), which is prepared by the condensation of citraconic anhydride and 1 : 2 : 4-trihydroxybenzene. This product resembles hydroxydroserone in its colour reactions, but differs from it markedly in that it is exceedingly difficult to crystallise. The experimental product is possibly a mixture of the 6- and the 7-methyl compound, and on account of the doubt as to its homogeneity its derivatives have not yet been investigated.



Of the tautomeric forms (V, VI) of hydroxydroserone, the second is regarded as the more stable in accordance with the evidence submitted in the previous papers. Hydroxydroserone thus falls into line with the structures of other well-known, naturally occurring hydroxynaphthaquinones such as lapachol (IX; Hooker, J., 1896, **69**, 1355; Fieser, J. *Amer. Chem. Soc.*, 1927, **49**, 857), lomatiol (X; Hooker, *loc. cit.*, p. 1381), and shikonin (XI; Majima and Kuroda, *Acta Phytochim.*, 1922, **1**, 43).



Shikonin presents a close parallel in its substituents to hydroxydroserone, and the formula proposed for the stable form of the compound is further supported by the fact that on heating shikonin gives a sublimate of 5-methylquinizarin.

EXPERIMENTAL.

3-Nitro-*o*-cresol (I).—*o*-Cresol (100 g.), dissolved in benzene (200 g.), was nitrated at 20° with nitric acid (530 g., *d* 1.21) (Schultz, *Ber.*, 1907, **40**, 4319); after the nitration additional benzene was added to assist in breaking down the emulsion. The benzene solution having been washed free from nitric acid, the mixture was steam distilled, giving almost pure 3-nitro-*o*-cresol, but if the distillation was prolonged some dinitro-compound also passed over. Repetition of the steam distillation gave the 3-nitro-derivative (20 g.) in a pure state; m. p. 67°.

An alternative method makes use of the nitrating action of excess of nitrous acid on diazonium compounds (Denninger, *J. pr. Chem.*, 1889, **40**, 299; Khotinsky and Jacopson-Jacopmann, *Ber.*, 1909, **42**, 3099). The best yield was obtained from *o*-toluidine (23 g.) dissolved in concentrated sulphuric acid (40 c.c.) and water (160 c.c.). The solution was cooled to 15°, and sodium nitrite (60 g.) in water (200 c.c.) added, gradually at first and then rapidly, the temperature being allowed to rise. The reaction mixture was poured at once into an excess of sulphuric acid (50%) contained in a large dish heated on a water-bath. After the vigorous evolution of gas had subsided, the mixture was steam distilled. Yield, 9.3 g. of pure product.

3-Nitro-2-methoxytoluene (II) and 2-methoxy-*m*-toluidine (III) were prepared by the methods of Shah, Bhatt, and Kanga (J., 1933, 1376). We found that these compounds boiled at 250° and 225° respectively, instead of 225° and 253° recorded by the above workers, who have evidently transposed the boiling points.

3 : 6-Dihydroxy-2-methoxytoluene (IV) was prepared by the method of Majima and Okazaki (*Ber.*, 1916, **49**, 1490). 2-Methoxy-*m*-toluidine (8 g.) in concentrated sulphuric acid (50 c.c.) and water (160 c.c.) was gradually treated with sodium dichromate (8 g.) in water (40 c.c.) with vigorous shaking at 3—5°. After 12 hours 16 g. of dichromate in water were added within the same temperature limits, and after several hours the mixture was repeatedly extracted with ether. After removal of the solvent the residue was steam distilled, and the distillate was saturated with sulphur dioxide, kept over-night, and repeatedly extracted with ether. Evaporation of the dried extract and recrystallisation of the residue from benzene gave (IV) as white needles (1 g.), m. p. 117—118°.

3 : 5 : 8-Trihydroxy-2-methyl-1 : 4-naphthaquinone (*Hydroxydroserone*) (V, VI).—The preceding quinol (1 g.), finely ground with an excess of maleic anhydride (2 g.), was added to a melt of anhydrous aluminium chloride (20 g.) and sodium chloride (4 g.) at 180°. The temperature rose spontaneously to 200° and was maintained at that point for about 5 minutes and then raised to 220°. The paste-like melt was dissolved in water and, after the addition of an equal volume of concentrated hydrochloric acid, heated till the purple-red colour had changed to dull red. The solid separating on cooling in ice was filtered off, and the filtrate extracted with chloroform. The solid after drying in a vacuum was boiled several times with chloroform until the extract was coloured only faintly yellow. The combined extracts were shaken with aqueous sodium hydroxide, which, when separated and acidified with hydrochloric acid, gave a bright scarlet, flocculent precipitate of the colouring matter. After one crystallisation from glacial acetic acid the product (0.5 g.) had m. p. 192—193°, alone or mixed with hydroxydroserone obtained from natural sources (Found : C, 59.8; H, 3.3. Calc. for C₁₁H₈O₅ : C, 60.0; H, 3.6%).

3 : 5 : 8-Triacetoxo-2-methyl-1 : 4-naphthaquinone.—Acetylation is best accomplished by treatment with acetic anhydride and a trace of anhydrous zinc chloride, the product being crystallised several times from benzene. After being heated in a vacuum tube in the vapour of boiling toluene to remove acetic acid of crystallisation, the triacetates from both the natural and the synthetic product had m. p. 152—153°, separately or mixed.

I wish to express my thanks to Professor Killen Macbeth for his interest in the work.

JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE. [Received, January 30th, 1935.]