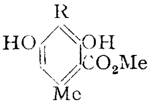
686. *The Application of the Modified Gattermann Reaction to Methyl and Ethyl Orsellinate.*

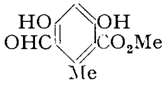
By W. B. Whalley.

Haematommic ester (I; R = CHO) is readily available by the application of the modified Gattermann reaction (Shah and Laiwalla, *J.*, 1938, 1828) to methyl orsellinate, and its conversion in high yield into atranol and β-orcinol provides a convenient alternative route to these rather difficultly accessible substances. Some derivatives of β-orcinol are described.

Although the structure of atranol has long been established (Robertson and Robinson, *J.*, 1927, 2196; Leon *et al.*, *ibid.*, 1931, 2697; St. Pfau, *Helv. Chim. Acta*, 1933, **16**, 282), this substance is not readily accessible. The synthesis recently described by Adams and Mathieu (*J. Amer. Chem. Soc.*, 1948, **70**, 2120) involves the very difficult demethylation of 2 : 6-dimethoxy-4-methylbenzaldehyde, and the application of the Gattermann synthesis to methyl orsellinate produces a difficulty separable mixture of the two aldehydes (I; R = CHO) and (II) in low yield (Robertson *et al.*, *J.*, 1933, 130; St. Pfau, *loc. cit.*). From (I; R = CHO) atranol was obtained by hydrolysis and decarboxylation. It has now been found that interaction of methyl orsellinate, zinc cyanide, and hydrogen chloride in the presence of aluminium chloride (Shah and Laiwalla, *loc. cit.*) gives an almost quantitative yield of methyl haematommate (I; R = CHO) unaccompanied by detectable amounts of the isomeride (II). Clemmensen reduction of atranol (cf. St. Pfau, *Helv. Chim. Acta*, 1926, **9**, 650) gives β-orcinol which is alternatively obtained by the reduction of (I; R = CHO), followed by hydrolytic decomposition of the resulting methyl β-orcinolcarboxylate (I; R = Me).



(I.)



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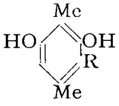

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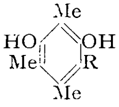

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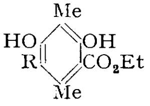

(V.)

In view of the availability of orsellinic ester (Sonn, *Ber.*, 1928, **61**, 926; St. Pfau, *Helv. Chim. Acta*, 1933, **16**, 282) a convenient novel route to β-orcinol, which is otherwise difficulty accessible (Kostanecki, *Ber.*, 1886, **19**, 2323; Robertson and Stephenson, *J.*, 1930, 313), is thus provided.

Reduction of 2 : 4-dihydroxy-3 : 6-dimethylbenzaldehyde (III; R = CHO) (St. Pfau, *Helv. Chim. Acta*, 1928, **11**, 864) by the Clemmensen method readily gave 2 : 4 : 5-*trimethylresorcinol* (III; R = Me) which was characterised by the formation of the *di*-p-*nitrobenzoate* and converted into the *aldehyde* (IV; R = CHO). On reduction the last-mentioned compound gave 2 : 4 : 5 : 6-tetramethylresorcinol (IV; R = Me) identical with a specimen prepared from 4 : 5 : 6-trimethylresorcinol (Robertson and Whalley, this vol., p. 3038). The non-identity of (IV; R = H) with 4 : 5 : 6-trimethylresorcinol (Robertson and Whalley, *loc. cit.*) provides further confirmation of the orientation of 4 : 5 : 6-trimethylresorcinol and hence of the structure of 2 : 4-dihydroxy-5 : 6-dimethylbenzaldehyde. Application of the Gattermann reaction to ethyl 2 : 4-dihydroxy-3 : 6-dimethylbenzoate (V; R = H) gave *ethyl* 2 : 4-*dihydroxy*-5-*formyl*-3 : 6-*dimethylbenzoate* (V; R = CHO).

EXPERIMENTAL.

Methyl 2 : 4-*Dihydroxy*-3-*formyl*-6-*methylbenzoate* (I; R = CHO).—Anhydrous aluminium chloride (8 g.), dissolved in ether (50 ml.), was slowly added (with stirring), at 0° to methyl orsellinate (3·8 g.) in ether (75 ml.) containing zinc cyanide (7 g.), the cooled mixture was saturated with hydrogen chloride, and 24 hours later the ethereal layer was decanted from a viscous oil, which was hydrolysed by heating it on the steam-bath for 20 minutes with water (100 ml.). On cooling, the hydrolysate deposited methyl haematommate (I; R = CHO) (3·0 g.) as a colourless, crystalline mass which, on recrystallisation from methyl alcohol, formed colourless needles, m. p. 146° (Found : C, 57·3; H, 4·7. Calc. for $C_{10}H_{10}O_5$: C, 57·1; H, 4·8%). Evaporation of the decanted ethereal solution, followed by hydrolysis, produced a further quantity (0·4 g.) of methyl haematommate (St. Pfau, *loc. cit.*, gives m. p. 147°). The ethyl ester was prepared by the same method and obtained in comparable yield.

Atranol.—When a mixture of the foregoing methyl or ethyl ester (1·5 g.), potassium hydroxide (5 g.), and water (30 ml.) was refluxed in an atmosphere of nitrogen for 2 hours, cooled and acidified, atranol separated as a pale buff, crystalline solid which crystallised from benzene–methanol in colourless needles (1·3 g.), m. p. 122°, soluble in sodium carbonate solution with the typical canary-yellow colour and giving an olive-green ferric reaction in alcohol (Found, for a specimen dried to constant weight : C, 63·3; H, 5·3. Calc. for $C_8H_8O_3$: C, 63·2; H, 5·3%).

β-Orcinol.—(*a*) Atranol (0·8 g.) in alcohol (12 ml.) was slowly added to concentrated hydrochloric acid (10 ml.) and water (5 ml.) containing zinc amalgam (15 g.), and the mixture refluxed for 30 minutes, diluted with water (100 ml.), and extracted with ether (5 × 50 ml.). Evaporation of the dried extracts gave β-orcinol in clusters of stout prisms (0·5 g.), m. p. 163°, identical with a specimen prepared by method (*b*).

(*b*) Methyl haematommate (1 g.) in methyl alcohol (40 ml.) was added during 15 minutes to gently boiling hydrochloric acid (30 ml.) (from 20 ml. of concentrated acid and 10 ml. of water) containing zinc amalgam (5 g.), and the mixture then heated under reflux for 30 minutes. The aqueous phase was removed by decantation, the residual amalgam washed with a little hot methyl alcohol, and the combined solution cooled, giving methyl β-orcinolcarboxylate (I; R = Me) which on crystallisation from aqueous methyl alcohol formed colourless needles (0·7 g.), m. p. 145°, exhibiting a reddish-brown ferric reaction (Found : C, 61·2; H, 6·4. Calc. for $C_{10}H_{12}O_4$: C, 61·2; H, 6·1%) (Sonn, *Ber.*, 1929, **62**, 3012, reports m. p. 141°). The ethyl ester was similarly prepared from ethyl haematommate.

A solution of the foregoing methyl or ethyl ester (0·5 g.), in potassium hydroxide (2 g.) and water (6 ml.) was refluxed in an atmosphere of nitrogen for 2 hours. Ether extraction of the acidified hydrolysate then gave β-orcinol (0·3 g.), crystallising from benzene–methyl alcohol in stout prisms, m. p. 163° (Found : C, 69·4; H, 7·2. Calc. for $C_8H_{10}O_2$: C, 69·6; H, 7·2%).

Ethyl 2 : 4-*Dihydroxy*-5-*formyl*-3 : 6-*dimethylbenzoate* (V; R = CHO).—When ethyl β-orcinolcarboxylate (V; R = H) (1 g.) in ether (100 ml.) containing zinc cyanide (2 g.) was subjected to the Gattermann aldehyde synthesis, the aldimine hydrochloride which separated during 24 hours was collected and hydrolysed on the steam-bath during 30 minutes, giving the 5-*formyl* ester (V; R = CHO) (0·7 g.), separating from ethyl alcohol in colourless needles, m. p. 137°, and exhibiting a reddish-brown ferric reaction (Found : C, 60·3; H, 5·6. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%). The 2 : 4-*dinitro*-

phenylhydrazone separated from ethyl acetate in silky, orange needles, m. p. 242° (decomp.) (Found: N, 13·1. $C_{18}H_{18}O_8N_4$ requires N, 13·4%).

2 : 4 : 5 : 6-*Tetramethylresorcinol.*—A solution of β-orcinaldehyde (4 g.) in methyl alcohol (40 ml.) was slowly added to a mixture of concentrated hydrochloric acid (30 ml.) and water (20 ml.) containing zinc amalgam (60 g.). After 1 hour's refluxing the mixture was diluted with water (200 ml.) and, after isolation with ether, 2 : 4 : 5-*trimethylresorcinol* (3 g.) separated from benzene in stellar aggregates of small prisms, m. p. 148° (Found: C, 71·3; H, 7·9. $C_9H_{12}O_2$ requires C, 71·1; H, 7·9%). The *di*-p-*nitrobenzoate* separated from glacial acetic acid in colourless needles, m. p. 223° (Found: N, 6·2. $C_{23}H_{18}O_8N_2$ requires N, 6·2%).

When the foregoing phenol (2 g.) in ether (100 ml.) containing zinc cyanide (4 g.) was saturated with hydrogen chloride at 0°, the aldimine hydrochloride separated during 24 hours and after hydrolysis with water (50 ml.) on the steam-bath during 30 minutes gave 6-*formyl*-2 : 4 : 5-*trimethylresorcinol* (IV; R = CHO) (1·7 g.) which separated from aqueous methyl alcohol in long, colourless needles, m. p. 181°, exhibiting a violet-brown ferric reaction (Found: C, 66·7; H, 6·9. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%). The 2 : 4-*dinitrophenylhydrazone* separated from much ethyl acetate as tiny, deep-crimson needles, m. p. 315—316° (decomp.) (Found: N, 15·2. $C_{16}H_{16}O_6N_4$ requires N, 15·6%).

The foregoing aldehyde (0·4 g.), in ethyl acetate (10 ml.) containing acetophenone (0·7 g.), was saturated with dry hydrogen chloride, giving 7-*hydroxy*-5 : 6 : 8-*trimethylflavylium chloride* which separated from very dilute hydrochloric acid in orange needles, m. p. 224° (decomp.) (Found: Cl, 11·5. $C_{18}H_{17}O_2Cl$ requires Cl, 11·8%).

When the previous aldehyde (0·5 g.), dissolved in methyl alcohol (25 ml.), was added to concentrated hydrochloric acid (20 ml.) and water (10 ml.) containing zinc amalgam (10 g.), and the mixture was refluxed for 30 minutes and then diluted with water, isolation with ether gave 2 : 4 : 5 : 6-tetramethylresorcinol (0·3 g.) which separated from light petroleum–benzene in colourless needles, m. p. 157° (after sublimation), identical with a specimen prepared from 4 : 5 : 6-trimethylresorcinol (Robertson and Whalley, *loc. cit.*). The di-*p*-nitrobenzoate crystallised from glacial acetic acid in colourless prisms, m. p. 226°, identical with an authentic specimen.

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