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A SYNTHESIS OF DIHYDROANHYDRO-O-TRIMETHYLBRAZILIN[1] AND SYNTHESIS OF dl-O-TETRAMETHYLBRAZILIN

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Previous methods of synthesis[2,3] of dihydroanhydro-O-trimethylbrazilin (III; R = OMe, R' = H) were difficult to be extended to synthesise brazilin (III; R = R' = OH) or its methyl ethers. Dihydroanhydro-O-trimethylbrazilin has now been synthesised by a new method and this method has been utilised to synthesise dl-O-tetramethylbrazilin. This appears to be the first synthesis of dl-O-tetramethylbrazilin; syntheses of d-brazilin[4] and dl-trimethylbrazilin[5] have recently been claimed.

In a recent note[3] I reported an easy synthesis of 2-carbethoxy-5,6-dimethoxyhydrindone-1 (I; R = H). Reduction of this compound with sodium and ethanol furnished 1-hydroxy-2-hydroxymethyl-5,6-dimethoxyhydrindene (II; R = H) as a sweet smelling viscous liquid. Condensation of this diol (II; R = H)

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[1] This compound is also known[2b] as dihydrodeoxytrimethylbrazilone or better as O-trimethylbrazilane.

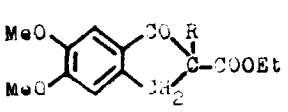
[2] (a) P.Pfeiffer, O.Angern, E.Haack and J.Willems, Ber. 61, 839 (1928); (b) W.H.Perkin, jun., W.N.Ray and R.Robinson, J.Chem.Soc. 1504 (1928).

[3] P.M.Chakrabarti, J.Proc.Inst.Chemists (India), 34, 264, (1962).

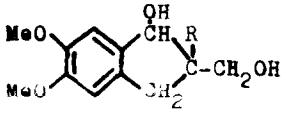
[4] F.Morsingh and R.Robinson, Int.Congress Pure and Appl. Chem., Zurich, 1953; Angew.Chem. 67, 761 (1955).

[5] O.Dann and H.Hofmann, Angew.Chem. 73, 535 (1961).

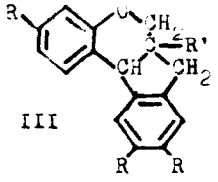
with resorcinol in glacial acetic acid by means of concentrated sulphuric acid followed by heating the product with dry ethanolic hydrogen chloride in a sealed bomb tube at 150° afforded a dark brown phenolic compound which on methylation with dimethyl sulphate and alkali followed by successive crystallisations from methyl alcohol furnished dihydroanhydro-O-trimethylbrazilin (III; R = OMe, R' = H) in colourless rod like needles, m.p. 108-9° alone or mixed with an authentic specimen prepared from anhydro-O-trimethylbrazilin by catalytic hydrogenation[2].



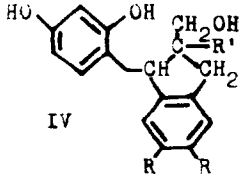
I



II



III



IV

Direct bromination of the alkali soluble ketoester (I; R = H) in carbon tetrachloride medium furnished an alkali insoluble noncrystalline bromo compound (I; R = Br), converted by dry sodium methoxide in boiling benzene into 2-carbethoxy-2, 5,6-trimethoxyhydrindone-1 (I; R = OMe) also insoluble in alkali, m.p. 220° - 24° (uncorr.) after slight softening at 215°. Reduction of this trimethoxy ketoester (I; R = OMe), in

suspension in ether, with lithium aluminium hydride yielded 1-hydroxy-2-hydroxymethyl-2,5,6-trimethoxyhydrindene (II; R = OMe), microscopic needles from methyl alcohol, m.p. 226-29° (uncorr.) with slight previous softening. Condensation of this diol (II; R = OMe) with resorcinol, in precisely the same way as was used in the case of the diol (II; R = H), followed by methylation with dimethyl sulphate and alkali afforded dl-O-tetramethylbrazilin (III; R = R' = OMe), m.p. 133-35°. The synthetic product behaved in a similar way as the natural O-tetramethylbrazilin towards decomposition reactions; the physical data are yet to be compared.

It is suggested that the primary reaction during the first stage of the condensation of the diol (II; R = H or OMe) with resorcinol, which takes place in glacial acetic acid in the presence of concentrated sulphuric acid, is a Friedel-Crafts alkylation involving elimination of water between the secondary hydroxyl group of the diol and the ortho-para hydrogen atom of the resorcinol nucleus leading to the formation of compounds of the type (IV; R = H or OMe); the second step is the usual chroman ring closure[6] between the primary alcoholic group and the phenolic -OH group by heating in a sealed tube with ethanolic hydrogen chloride. Friedel-Crafts alkylation of phenols with benzyl alcohol by means of sulphuric acid in glacial acetic acid is known[7]. Ordinary alcohols do not alkylate under similar conditions.

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[6] F.W.Semmler, Ber. 39, 2851 (1906).

[7] E.Paterno and M.Fileti, Gazzetta, 5, 381; J.Chem.Soc. Abs. 29, i, 581 (1876).