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SUBSTITUTION *META*- TO AN AROMATIC HYDROXYL GROUP

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Abstract: It is suggested that the bromination of 4-methylphenol in superacid solvents involves a 1,2-shift of bromine within a protonated bromodienone.

The bromination of 4-methylphenol (1) in HF-SbF_5 has been shown[1] to give 3-bromo-4-methylphenol (2), and it was suggested that this reaction involves protonation of the hydroxyl group to give the O-protonated cation (3), in which the substituents might each direct the entering reagent to the 3-position. It was considered[1] that C-protonated forms of the phenol (e.g., 4), known to be formed from 4-methylphenol in some superacid solvents,[2,3,4] would be unreactive.

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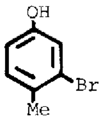

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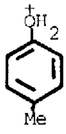

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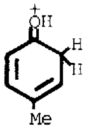

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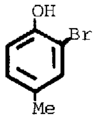

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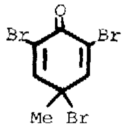
When 4-methylphenol is dissolved in trifluoromethanesulphonic acid its ^1H n.m.r. spectrum consists of a signal attributable to the methyl group at δ1.95 and a broad, unresolved signal at δ6.80 integrating for rather less than three protons. This is not the spectrum expected for 1 or 2; instead, it is that expected for 4, with the 2- and 6-protons exchanging rapidly with the medium.

This solution (*ca.* 0.5*M*) was treated with bromine (1 mol. equiv.). Rapid reaction occurred, and hydrogen bromide was evolved. The ^1H n.m.r. spectrum of the reaction mixture was examined at intervals, and aliquot parts were removed for concurrent recovery of the products and study of their ^1H n.m.r. spectrum. The product formed under kinetic control (after about 10 min.) contained 2 (*ca.* 60%) and 2-bromo-4-methylphenol (*ca.* 40%). It was slowly converted ($t_{½}$, *ca.* 20h) into a thermodynamically controlled mixture containing *ca.* 90% of 2.

Bromination of 4-methylphenol in trifluoromethanesulphonic acid could be effected also, but with rather more difficulty, by using N-bromosuccinimide as the source of electrophilic bromine. When either 2 or 5 was dissolved in trifluoromethanesulphonic acid, a slow rearrangement occurred over the course of several days to give a mixture of the two, containing also some 4-methylphenol formed by protodebromination.

Bromodienones (e.g., 6) are known to undergo acid-catalysed rearrangement by 1,2-shifts of bromine,[5,6] and we have shown that 6 when treated with trifluoromethanesulphonic acid is rapidly converted into the phenol 7. These results suggest to us that the 3-bromination of 4-methylphenol may occur by a pathway different from that envisaged by Jacquesy et al.[1] Since we know that 4 is formed rapidly, it can be expected that the protonated bromodienone 8 would be formed also in the presence of bromine. Of the three pathways open to it (giving 5, 9, and 10 respectively), the rearrangement to give 10 and thence protonated 3-bromo-4-methylphenol is faster than proton-loss from carbon to give 5, whilst proton-loss from oxygen is so effectively reversed by the strongly acid conditions that 2-bromo-4-methylphenol cannot be formed through the unprotonated *ortho-* dienone 9, as it is when the acidity is less.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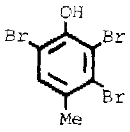
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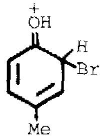
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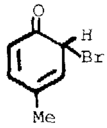
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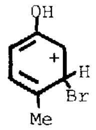
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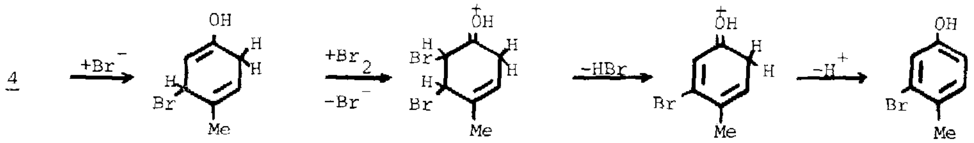
A modification of this pathway would involve bromination *ipso-* to the methyl group to give a protonated 2,5-dienone instead of the protonated 3,5-dienone 8. Either of these pathways would allow reversible interconversion of the two phenols 2 and 5 proceeding slowly because in trifluoromethanesulphonic acid they would be most stable as the protonated species.

Yet another way in which bromine could reach a position *meta-* to the hydroxyl group would involve an addition-elimination sequence.



It is well known, for example, that the brominations of $\alpha\beta$-unsaturated ketones and of quinones are powerfully catalysed by hydrogen bromide.[7] Such a mechanism seems unlikely, however, for bromination by N-bromosuccinimide.

The experiments reported here do not disprove Jacquesy et al's view[1] of the reason for bromination *meta-* to an aromatic hydroxyl group in superacid solvents; but the pathways which we propose as alternatives seem more in keeping with other known chemistry, including the fact that the OH_2^+ group is likely to be *ortho*, *para-* rather than *meta*-directing by analogy with the known chemistry of the OPh_3^+ group.[8]

The nature of the brominating species providing positive bromine under the strongly acidic conditions used in this work is not known; it may be Br_2 or HBr_2^+, and is unlikely to be an oxidised state of bromine, since iodine has been reported[9] to form a violet solution in trifluoromethanesulphonic acid and to give oxidized states of iodine only when treated with a strong oxidizing agent.

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