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ELECTROPHILIC ALLYLATION OF 2,6-DIMETHYLPHENOL AND 2,6-DIMETHYLANISOLE AT META-POSITIONS

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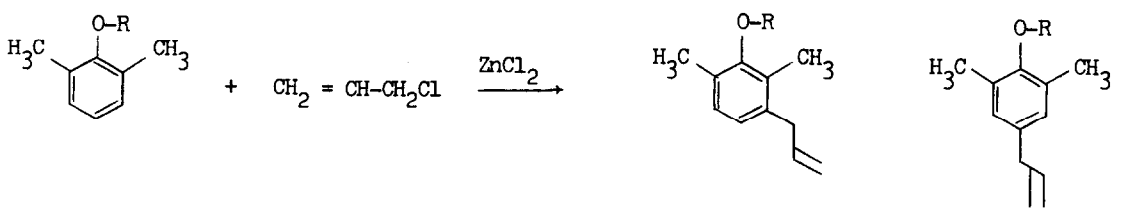
Electrophilic benzylations of 2,6-dimethylphenol and its ethers give surprisingly high yields of products of attack at meta-positions of the aromatic rings.[1] Examination of possible mechanisms for meta-benzylation showed that only direct attack at the meta-positions was consistent with all the evidence. In particular, the possibility that benzylation initially occurred at ortho-positions was ruled out for reactions of 2,6-dimethylphenyl ethers, and, by analogy, for reactions of 2,6-dimethylphenol.[1]

We have now investigated the Friedel-Crafts allylation of 2,6-dimethylphenol (2,6-DMP) and 2,6-dimethylanisole (2,6-DMA), and have found that unexpectedly high yields of meta-substitution products are again obtained. We have demonstrated that initial attack at ortho-positions of 2,6-DMP can account for no more than a small percentage of the yield of meta-allylation product.

No reaction could be detected between allyl alcohol and 2,6-DMP in a 4M solution of sulfuric acid in ether at room temperature, while refluxing a chloroform solution of 2,6-DMP and either allyl bromide or allyl chloride in the presence of zinc chloride[1] gave complex mixtures from which no identifiable products could be isolated. If, however, allyl chloride was added very slowly to a refluxing solution of 2,6-DMP in chloroform containing zinc chloride, a clean reaction occurred to give two products which appeared as overlapping peaks on glpc analysis. Hydrogenation of the allyl groups to propyl groups resulted in separation of the two peaks. Glpc analysis showed the hydrogenation products to consist of 2,6-dimethyl-3-propylphenol (24%) and 2,6-dimethyl-4-propylphenol. The products were identified by addition of sufficient bromine to react with the 2,6-



24%, R = H
60%, R = CH_3

76%, R = H
40%, R = CH_3

dimethyl-3-propylphenol. The components of the mixture were then isolated and identified as 4-bromo-2,6-dimethyl-3-propylphenol and 2,6-dimethyl-4-propylphenol by comparison with independently prepared samples.

Reaction of allyl chloride with 2,6-DMA in the presence of zinc chloride in refluxing chloroform proceeded without difficulty to give a mixture of two products. Hydrogenation of the mixture, bromination of the major component, and glpc isolation of the resulting products yielded 4-bromo-2,6-dimethyl-3-propylanisole and 2,6-dimethyl-4-propylanisole, whose structures were established by comparison with independently prepared samples. Glpc analysis of the mixture of allylation products after hydrogenation showed it to contain 59.9 ± 0.3% of the meta-substituted isomer.

Reaction of 2,6-DMA with allyl bromide under the same conditions gave a mixture of halogen-containing products. Dehydrohalogenation with potassium t-butoxide in t-butanol, hydrogenation of the resulting olefins, and bromination of the major isomer gave the same products obtained from reaction with allyl chloride. The meta-isomer again comprised 60% of the product.

To determine whether meta-allylation products had been formed by initial ortho-attack followed by 1,2-allyl migrations, 6-allyl-2,6-dimethylcyclohex-2,4-dien-1-one, the product which would be obtained by ortho-allylation of 2,6-DMP, was heated in refluxing chloroform in the presence of zinc chloride and allyl chloride. Rearrangement was complete in 5 minutes,[2] and was found to yield a mixture of which 96.5% was 4-allyl-2,6-dimethylphenol. Thus, almost all the meta-isomer formed during allylation of 2,6-DMP must have been formed by direct attack at meta-positions, rather than by initial attack at an ortho position. Indeed, the lower percentage of meta-allylation of 2,6-DMP compared to the percentage of meta-benzylation suggests the possibility that some of the para-allylated product may have arisen by initial ortho-attack.

It has been suggested[3] that Friedel-Crafts alkylations proceed by "early" transition states. It is conceivable that in such reactions the resonance effects of oxygen atoms, reduced by steric inhibition of resonance in 2,6-DMA and poor solvation of the hydroxy group in 2,6-DMP, might be swamped by the inductive effects of the methyl groups, while in reactions with late transition states resonance effects may be predominant. As yet, however, no evidence is available to distinguish between this and other possible explanations for the high yields of meta-substitution products from allylation and benzylation of 2,6-DMP and its ethers.

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References

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3) G. A. Olah and S. Kobayashi, J. Am. Chem. Soc., 93, 6964 (1971)

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