A Novel Route to Resorcinols

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Summary Hydroxylation of *para*-alkylated or 2,6-dialkylated phenols by hydrogen peroxide in SbF_5–HF yields resorcinols, the electrophile reacting with the *O*-protonated substrate

ELECTROPHILIC hydroxylation of aromatic compounds has received considerable attention in the last decade[1,2] and it has been reported that under acidic conditions phenols are readily converted into hydroquinones and catechols [3] We report here our results on the reaction of phenols with hydrogen peroxide in SbF_5–HF (see Table) All substrates yield the *meta*-hydroxy-derivatives in fair to excellent yields

The structures of the products, and the relative migratory aptitudes of methyl and hydroxy groups[4] rule out an initial

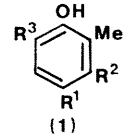
TABLE.[a]

Starting material	Molar ratio SbF_5: HF	Products (% yield)[b]
(**1a**)	0·02 : 1	(**1b**) (17) + (**1c**) (4) + (**1d**) (3) + (**2b**) (3) + (**1a**) (70)
(**2a**)	0·04 : 1	(**2b**) (78) + (**2a**) (15)
(**3a**)	0·04 : 1	(**3b**) (58) + (**3c**) (32) + (**3a**) (5)
(**4a**)	0·04 : 1	(**4b**) (88) + (**4a**) (4)
(**5a**)	0·02 : 1	(**3c**) (29) + (**5b**) (4) + (**5a**) (45)

[a] Reactions were performed at −40 °C. Hydrogen peroxide (30 or 95%) was added to a solution of the substrate in SbF_5–HF. Reaction times were 30 min for the phenols. Similar results were obtained for the corresponding ethers after a reaction time of 5 min. Molar ratios using 95% H_2O_2 were SbF_5: substrate 6 : 1; H_2O_2: ether 1·2 : 1; H_2O_2: phenol 1·4 : 1; and using 30% H_2O_2 were SbF_5: substrate 16—18 : 1; H_2O_2: ether 1·3 : 1; H_2O_2: phenol 1·5 : 1. For *o*-cresol (**1a**), the H_2O_2: substrate molar ratio was 2 : 1. [b] Yields are identical, using 30 or 95% H_2O_2 and are for isolated products after purification by column chromatography over SiO_2.

reaction in the *ortho*- or *para*-position followed by rearrangement; thus only a direct *meta*-hydroxylation accounts for the formation of resorcinols.

These results can be explained by considering the equilibrium between the neutral substrate and its protonated forms, the electrophile ($H_3O_2^+$, or OH^+ equivalent)[2,5] reacting either on the neutral or on the oxygen protonated form[6] of the substrate.



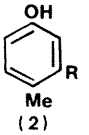
(1)

a; $R^1=R^2=R^3=H$

b; $R^1=OH, R^2=R^3=H$

c; $R^1=R^2=H, R^3=OH$

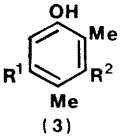
d; $R^1=R^3=H, R^2=OH$



(2)

a; R = H

b; R = OH

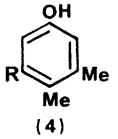


(3)

a; $R^1=R^2=H$

b; $R^1=OH, R^2=H$

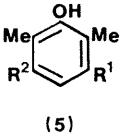
c; $R^1=H, R^2=OH$



(4)

a; R = H

b; R = OH



(5)

a; $R^1=R^2=H$

b; $R^1=R^2=OH$

Ring substitution in compounds (**2**—**5a**) favours O-protonation,[6,7] the co-operative effect of the methyl and the protonated hydroxy-groups directing the electrophilic attack to the *meta*-position. The high acidity of the medium and the basicity of the products protect them from further oxidation, a drawback of such hydroxylations under normal acidic conditions.[8]

In contrast, for phenol (H_2O_2: phenol 2 : 1) and to a lesser extent for compound (**1a**), O-protonation is disfavoured relative to C-protonation and the reaction occurs on the neutral substrate whose concentration is always small under these conditions.† Therefore the reaction is slow with predominant formation of *ortho*- and *para*-hydroxy derivatives in accordance with a typical electrophilic aromatic substitution. For the more basic *m*-cresol, C-protonation of the ring is highly favoured, thus preventing any hydroxylation.

As expected, the corresponding methyl ethers give similar results but exhibit a higher reactivity, an effect already observed in the bromination of these compounds.[6]

This new reaction appears to be very attractive for preparation of substituted resorcinols and shows that, under very acidic conditions, the *meta*-position of phenolic compounds is the most reactive with electrophiles.

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† Under more acidic conditions (FSO_3H–SbF_5, 1 : 1), it has been reported that phenol and anisole are unreactive (ref. 4).

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