Oxidation of Simple Phenols by a Homobimetallic Cerium(IV)–Calix(8)arene Complex in Conjunction with Hydrogen Peroxide

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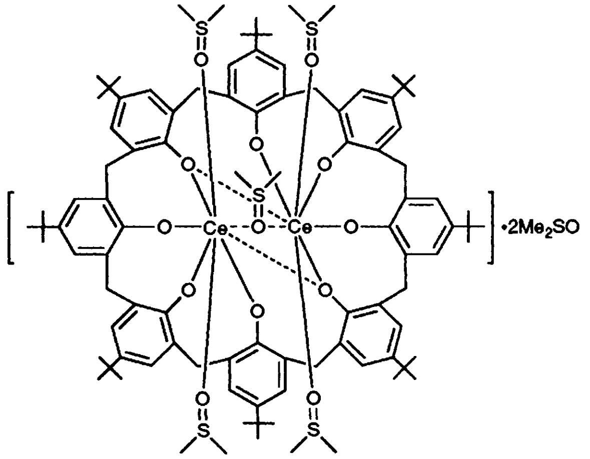
Phenolic substrates are regioselectively hydroxylated under mild conditions with a cerium(IV)–calix(8)arene complex.

There are few methods to promote direct hydroxylation of aromatic substrates.[1–7] The yields in such reactions are generally poor probably owing to further oxidation of the resulting phenols. We report herein a novel method for the regioselective hydroxylation of phenolic substrates under mild reaction conditions† (Table 1) by a homobimetallic complex **1** obtained by the reaction of cerium(IV) ammonium nitrate with *p-tert*-butylcalix(8)arene, H_8L.[8,9]

The reaction is facile and regioselective (Table 1). For instance, only hydroquinone is obtained, with no 1,2-benzenediol or 1,4-benzoquinone formed. Similarly, other phenols (entries 2–5 in Table 1) gave only one isolable hydroxylation product. Salicylaldehyde (entry no.8) gave 1,4-benzenediol and 1,2-benzenediol along with a small amount of 2-hydroxybenzoic acid as the only products thereby indicating that the oxidation may be accompanied by decarboxylation as previously observed[7] or may involve a Dakin-type reaction though the latter almost always requires alkaline conditions[10] which were not used in the present investigation. Toluene and anisole failed to yield the hydroxylation products demonstrating the need for a phenolic group in the substrate, *cf.* refs. 3, 4. In general, it has been observed that the newly introduced hydroxy group prefers a position *para* to the hydroxy group already present in the substrate.

No hydroxylated product could be isolated when H_2O_2 or the complex salt was omitted or used without the complex. Detailed analysis of the reaction mixture revealed that the reaction also yields cerium(IV) hydroxide/oxide and calix(8)arene as side products which can be recycled. Semiquantitative experiments revealed that 0.5 mol of the complex is sufficient for oxidation of 1 mol of the phenolic substrate and when excess of the reagent was employed it leads to further hydroxylation and oxidation of alkyl groups present (if any).



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In all the eight examples studied, the product of hydroxylation is not accompanied by polymers which are the usual outcome of oxidation reactions of phenolic substrates. The method therefore is unique and exemplifies the first hydroxylation procedure where further oxygenation is inhibited (entry 2, Table 1, is an exception).

The authors thank the Departments of Science & Technology and Biotechnology for financial assistance.

Received, 13th August 1993; Com. 3/04918C

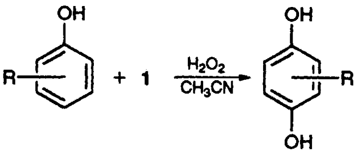

Table 1

Entry	Reactant	Product[a]	Yield[b] (%)	Mp/°C	Lit.Mp[d] (°C)
1	Phenol	1,4-Benzenediol	40	172–173	172
2	2,5-Dimethylphenol	2,5-Dimethyl-1,4-benzoquinone	38	123–125	125
3	2,6-Dimethylphenol	2,6-Dimethyl-1,4-benzenediol	44[c]	149–151	149–151
4	Resorcinol	1,2,4-Benzenetriol	42	139–140	140.5
5	Hydroquinone	1,2,4-Benzenetriol	39	139–140	140.5
6	Toluene	No product	—		
7	Anisole	No product	—		
8	Salicylaldehyde	1,4-Benzenediol	28	172–173	172
		1,2-Benzenediol	26	103–106	105
		2-Hydroxy benzoic acid	20	158–160	159

[a] All compounds were identified by comparison with authentic samples and spectral characterization. [b] The yields mentioned are isolated yields and unoptimized. [c] Yield increases to 56% at substrate : oxidant ratio of 1:1. [d] *Dictionary of Organic Compounds*, 5th edn. Chapman and Hall, New York, 1982.

Footnote

† *Typical procedure*: H_2O_2 (5 ml) was added at room temp. to stirred MeCN (100 μl) containing $[(Ce_2L)(Me_2SO)_5]\cdot 2Me_2SO$ (0.5 mmol) and 2,6-dimethylphenol (1.0 mmol). The mixture was stirred for 4–5 h, filtered and evaporated. The residue was heated under reflux for 2–3 h in methanol. Evaporation and crystallisation gave 2,6-dimethylbenzene-1,2-diol.

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