ipso-Attack in the Hydroxylation of *o*- and *p*-Xylene using bis(trimethylsilyl) Peroxide and Aluminium Chloride

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Summary Electrophilic hydroxylation of *o*- and *p*-xylene using a range of peroxides, including the title compound, in the presence of Lewis acids results in the formation of mixtures of phenols including those derived by *ipso*-attack followed by rearrangement; *ipso*-attack by the hydroxyl radical leads to dealkylation.

HYDROXYLATION reactions of benzene and simple alkylbenzenes using hydrogen peroxide and various catalyst systems have been reported.[1] Cationic reagents were suggested. t-Butyl hydroperoxide in the presence of aluminium chloride has also been used and the electrophile was suspected to be the t-butoxy-cation.[2] In all of the reactions using toluene as the substrate[1,2] a high $o:p$ ratio was observed but this does not allow a distinction to be made with respect to electrophilic radical hydroxylation; for example Fenton's reagent[3a] and peroxydisulphate [3b] afford cresols in similar ratios.† *ipso*-Attack followed by rearrangement occurs with a number of highly alkylated arenes using trifluoroperacetic acid and boron trifluoride.[4] Thus hexamethylbenzene affords hexamethylcyclohexa-2,4-dienone in 95% yield.

We now report the preliminary results of our studies of the hydroxylation reactions of the isomeric xylenes using Fenton's reagent and bis(trimethylsilyl) peroxide[5] in the presence of aluminium chloride. Bis(trimethylsilyl) peroxide has been used previously in a number of oxidation reactions as a protected form of hydrogen peroxide.[6] Although optimum conditions have not been established for the reactions with the silicon compound, important differences are evident from a comparison of these results with those obtained using Fenton's reagent (Table). Analysis of the recovered xylenes and control experiments using the xylenols established that *o*- and *p*-xylene and the xylenols did not isomerise in the presence of aluminium chloride under the conditions used.

ipso-Attack followed by rearrangement is a well established route involving a number of cationic reagents.[7] Recent work has also established that *ipso*-attack can also occur with radicals,[8] including the displacement of alkoxy-groups by means of the benzyloxyl radical.[9] Alkyl migration in an *ipso*-arenium ion is facilitated by the relatively low energy of the transition state leading to the new arenium ion (a protonated cyclohexa-2,4-dienone) that can re-aromatise by loss of a proton (equation 1) although we should not rule out the possibility that arene-oxides are involved in these reactions.[10] Conversely, the *ipso*-dealkylation reactions observed using Fenton's reagent presumably

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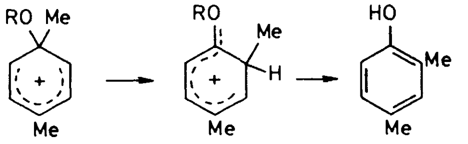
† In an important paper published since the submission of the manuscript (T. Tezuka, N. Narita, W. Ando, and S. Oae, *J. Am. Chem. Soc.*, 1981, **103**, 3045) new isomer distribution ratios have been reported for the hydroxyl radical hydroxylation of toluene and a number of other mono-substituted benzene derivatives using the photodecomposition of an α-azohydroperoxide as the source of the hydroxyl radical.

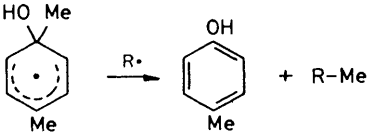
TABLE. Hydroxylation of xylenes.

Substrate	Reagent (mol ratio)	% Yield	Isomer distribution of xylenols[a] (%)	Cresol[a] (%)	k_H/k_{ipso}
p-xylene	$\mathrm{Bu^tOOH/AlCl_3}$ (1:2)	40	(2,5) 70:(2,4) 30	0·0	1·1
p-xylene	$\mathrm{(PhCH_2OCOO)_2/AlCl_3}$ (1:2)	19	(2,5) 70:(2,4) 30	0·0	1·1
p-xylene	$\mathrm{(Bu^tOO)_2CO/AlCl_3}$ (1:4)	20	(2,5) 66:(2,4) 34	0·0	0·9
p-xylene	$\mathrm{[Me_3SiO]_2/AlCl_3}$ (1:2)	18	(2.5) 69:(2,4) 31	0·0	1·1
p-xylene	$\mathrm{Fe^{2+}/H_2O_2}$	—	(2,5) 24	76	0·1
o-xylene	$\mathrm{Bu^tOOH/AlCl_3}$ (1:2)	50	(2,3) 26:(3,4) 60:(2,6) 5	9	8·6
o-xylene	$\mathrm{Bu^tOOH/TiCl_4}$ (1:3)	49	(2,3) 17:(3,4) 83:(2,6) $<$ 0·5	0·0	∞
o-xylene	$\mathrm{[Me_3SiO]_2/AlCl_3}$ (1:2)	22	(2,3) 38:(3,4) 45:(2,6) 17	0·0	2·4
o-xylene	$\mathrm{Fe^{2+}/H_2O_2}$	—	(2,3) 12:(3,4) 15	73	0·1
m-xylene	$\mathrm{Bu^tOOH/AlCl_3}$ (1:2)	41	(2,4) 83:(2,6) 15:(3,5) 2	0·0	∞
m-xylene	$\mathrm{[Me_3SiO]_2/AlCl_3}$ (1:3)	26	(2,4) 73:(2,6) 25:(3,5) 2	0·0	∞
m-xylene	$\mathrm{Fe^{2+}/H_2O_2}$	—	(2,4) 56:(2,6) 14:(3,5) 3	27	1·3

[a] The phenolic products were analysed by gas chromatography, using, in the reactions involving *o*- and *m*-xylene a 25 m CPWax 51 capillary column, and in the reactions involving *p*-xylene a 25 m OV 1 capillary column.



(1)



(2)

reflect the high energy of the transition states that would be involved if rearrangement occurred, as compared with that involved in dealkylation by the same or another radical (equation 2). Thus we can distinguish between hydroxylation reactions involving radicals and cations.

An inspection of k_H/k_{ipso}values for the reactions of *o*- and *p*-xylene with bis(trimethylsilyl) peroxide and aluminium chloride reveals a remarkably low value for *p*-xylene (1·1). The results from studies using aqueous hydrogen peroxide and pyridinium polyhydrogen fluoride at 0 °C,[1d] gives a value for *p*-xylene ($k_H/k_{ipso} = 3{\cdot}4$) but we should note that using this system some radical hydroxylation–dealkylation was observed. The value for *o*-xylene was 12 as compared with our value of 2·4. These differences may result from different steric requirements of the different reagents. It is not surprising that greater positional selectivity was observed[1c] at lower temperatures. At −78 °C the k_H/k_{ipso} values for *p*-xylene and *o*-xylene are 0·9 and 3·6 respectively. A further difference between our results and those reported previously is seen by inspection of the ratio of 2,3- to 3,4-xylenol in reactions of *o*-xylene.

Indeed the k_H/k_{ipso} values may not be meaningful in this case since two successive alkyl shifts could give, after proton loss, 2,3-xylenol. An alternative explanation is that the electrophile involved in the reactions reported here is larger and hence a more sterically demanding species.

The precise nature of the electrophile involved in a number of the hydroxylation reactions is obscure. However, it is clear that in reactions using t-butyl hydroperoxide it is not the t-butoxy-cation. A number of potential routes to this ion have been investigated and in no case was significant hydroxylation observed. These include t-butyl hydroperoxide and trifluoromethanesulphonic anhydride, t-butyl hypochlorite and silver(I) salts, and t-butyl chloroperformate and silver(I) salts. The facility with which rearrangement to the dimethyl methoxycarbenium ion occurs has also been demonstrated in the reactions of t-butyl hydroperoxide with 'magic acid' and of the trimethylcarbenium ion with ozone.[11]

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