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FRONTIER ORBITAL CONTROL FOR THE HYDROXYL RADICAL ATTACK ON AROMATICS

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The ortho:meta:para isomer ratio and p/m value observed in the aromatic hydroxylation with hydroxyl radical in anhydrous organic media are correlated with the electron density of HOMO of aromatics.

The hydroxyl radical is thought to be an electrophilic species and to attack predominantly at the ortho and para positions of aromatics having an electron-donating substituent.[1,2] However, it seems that attempts to predict the isomer ratio of phenols by the theoretically deduced reaction indices have not been successful.[3] This is in part due to that the isomer ratio varies with the different reaction conditions employed in the reaction with Fenton's reagent or by radiolysis in aqueous media, and hence various isomer ratios were reported.[1-4]

Recently, we obtained new isomer ratios of phenols (3) in the reaction with hydroxyl radical generated from α-azohydroperoxide (1) in anhydrous organic media. Several control tests indicated that the isomer ratio of phenols observed by us reflects correctly the extent of the position of aromatics attacked by hydroxyl radical.[4,5] On the basis of this new isomer ratio, we examined whether or not the observed isomer ratio can be correlated with MO quantities. We report in this paper that the isomer ratios are correlated with the electron densities of

Scheme 1

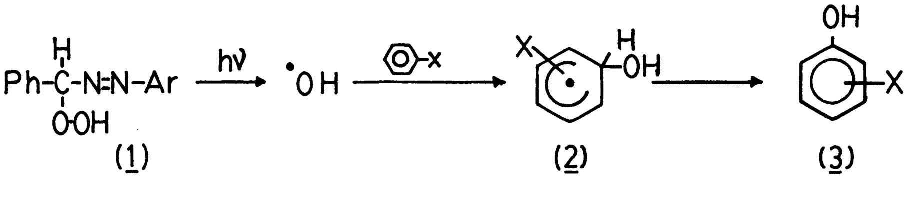

Table 1. Observed isomer ratios of phenols

3	o	:	m	:	p
Hydroxyanisole	82	:	1	:	17
Cresol	65	:	12	:	23
Chlorophenol	38	:	23	:	39
Nitrophenol	28	:	47	:	25

the HOMO of aromatics.

The standard isomer distribution ratios of hydroxyanisole, cresol, chlorophenol, and nitrophenol obtained by the hydroxylation of anisole, toluene, chlorobenzene, and nitrobenzene with hydroxyl radical generated from 1 in anhydrous media under argon are indicated in Table 1. These values were obtained by carrying out several control experiments under argon in the absence and presence of oxidants for cyclohexadienyl radical intermediates (2).4,5) The error allowance is less than 10%.

The total π-electron density (HMO), P_z-AO population (CNDO/2),6) free valence (HMO), and atomic population (CNDO/2) for anisole, toluene, chlorobenzene, and nitrobenzene were compared with the observations. However, both p/m values and the o:m:p ratios obtained from these indices were found not to correlate with the experimental values (see Table 2).

Next, the frontier electron densities (CNDO/2) of the electrophilic (f_r^{HO}), nucleophilic (f_r^{LU}), and radical (f_r^{HO+LU}) reactions were compared.7) The p/m values ($[p/m]^{HO}$, $[p/m]^{LU}$, and $[p/m]^{HO+LU}$) were obtained from these electron densities by using equation 1, where f_m^k, $f_{m'}^k$, and f_p^k are frontier electron densities at the 3, 5, and 4 positions of the aromatics respectively; k is either a HOMO, LUMO, or [HOMO+LUMO]. It is clear from the table that the p/m values obtained from the

$$[p/m]^k = f_p^k \ / \ (f_m^k + f_{m'}^k) \qquad (1)$$

electron density of the HOMO ($[p/m]^{HO}$) best correlate with the observed values. Neither $[p/m]^{LU}$ nor $[p/m]^{HO+LU}$ shows a correlation. It is important to point out that the HOMO electron density predicts well the site of the hydroxyl radical attack on aromatics, but neither the total π-electron density nor the radical reaction index is correlated with the observations. In addition, the π-orbitals low-

Table 2. p/m values observed[a)] and calculated[b)]

X	OCH_3	CH_3	Cl	NO_2
Observation[a]	17.00	1.92	1.70	0.53
π-electron density[b]	0.53	0.51	0.51	0.47
Pz-AO population[b]	0.53	0.52	0.49	0.49
Atomic population[b]	0.51	0.50	0.50	0.50
$[p/m]^{HO\,b}$	3.12	2.70	2.81	0.17
$[p/m]^{LU\,b}$	0.00	2.12	2.58	3.25
$[p/m]^{HO+LU\,b}$	0.41	2.37	2.66	3.22

a) Obtained by the observed isomer ratios of phenols.
b) Deduced from the electron distribution at ortho, meta, and para positions of aromatics.

er than the HOMO were found not to correlate with the observations.

The delocalization energy and SOMO energy (CNDO/2) of the ortho-, meta-, and para-oriented hydroxycyclohexadienyl radicals (2), which are formed by the attack of hydroxyl radical on aromatics, were found not to correlate with the observed values. This is inconsistent with the results obtained by Eberhardt and Yoshida on the basis of the data in aqueous media.[3)] In addition, the superdelocalizability (HMO) was also found not to correlate with the observed values.

Meanwhile, Fleming proposed that the (o+2p)/m value in the free radical aromatic substitution increases with decreasing of the SOMO energy of the attacking radicals.[8)] The (o+2p)/m value for the hydroxylation of anisole observed in the present study is 116. This is a highest value among those of free radical phenylation (5.3), methylation (6.2), and carboxymethylation (25) of anisole.[3,8,9,10)] Similar trends were identified in the case of toluene.[10)] These indicate that hydroxyl radical is the strongest ortho- and para-attacking radical among others for aromatics having an electron-donating substituent. This is probably due to the fact that hydroxyl radical has an extremely low SOMO energy (IP = 13.2 eV) compared with the other radicals.[11)]

It is suggested that the ortho-isomer ratio of phenols is influenced by the substituent group.[12)] Even if we take this into account and use the p/m value instead of the (o+2p)/m for comparison, the para-attacking property of hydroxyl radical for anisole, toluene, and chlorobenzene and/or the meta-attacking for nitrobenzene is still apparent. In summary, the present study revealed first time that the HOMO of aromatics strongly controls the site of the hydroxyl radical attack on the aromatic ring. From this point of view, the hydroxyl radical is an electrophilic species.

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