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A DFT Study on Intramolecular Hydrogen Bond in Substituted Catechols and Their Radicals

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Abstract: Density functional theory (DFT) at B3LYP/6-31G(d,p) level was employed to calculate intramolecular hydrogen bond enthalpies (H_{IHB}), O-H charge differences, O-H bond lengths and bond orders for various substituted catechols and their radicals generated after H-abstraction. It was found that although the charge difference between hydrogen-bonded H and O played a role in determining H_{IHB}, H_{IHB} was mainly governed by the hydrogen bond length. As the oxygen-centered radical has great tendency to form a chemical bond with the H atom, hydrogen bond lengths in catecholic radicals are systematically shorter than those in catechols. Hence, the H_{IHB} for the former are higher than those for the latter.

Keywords: Catechol, catecholic radical, density functional theory, intramolecular hydrogen bond.

Phenolic antioxidants (ArOH) have been extensively used in chemical industry, food industry and pharmaceutical industry[1-3]. In many cases, ArOH scavenge free radicals through donating a hydrogen atom[4]. Thus, the O-H bond dissociation enthalpy (BDE) becomes an important parameter to characterize the radical scavenging activity[5-8]. The lower the O-H BDE is, the higher the antioxidant activity.

As known to all, catechol is the active center for natural phenolic antioxidants[9,10], because of its low O-H BDE. A few preliminary theoretical studies indicated that the low O-H BDE of catechol stemmed from two effects, the electronic effect and the intramolecular hydrogen bond (IHB) effect, both of which contributed approximately 20 kJ/mol to reduce the O-H BDE[11,12]. The former effect resulted from the electron-donating property of the *ortho* hydroxyl group, while the latter resulted from the higher IHB enthalpy (H_{IHB}) for catecholic radical than that for parent catechol[11,12]. Therefore, IHB plays an important role in enhancing natural antioxidant activity. However, there exist controversial results related to the IHB in catechols and their radicals. For instance, based on the thermal decomposition study of substituted anisoles[13], the H_{IHB} for catecholic radical can be estimated higher than 9.0×4.184 kJ/mol, just in line with the theoretical value. But a recent EPR equilibration experiment showed that the H_{IHB} of catecholic radical was only 4.4×4.184 kJ/mol, near to the H_{IHB} of parent catechol[14],

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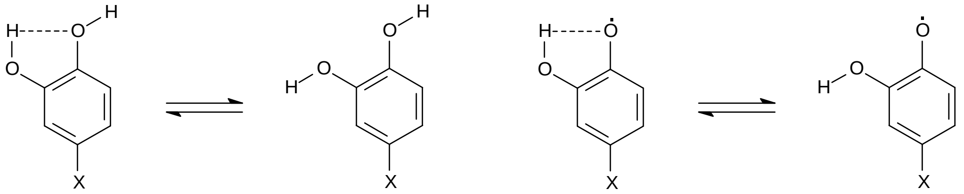
which meant that the IHB effect to reduce O-H BDE would be near to zero. Apparently, further study is needed to elucidate the discrepancy. In this letter, we attempt to calculate the H_{IHB} for substituted catechols and their radicals by high level density functional theory (DFT) method and to investigate the factors determining H_{IHB}.

Methods

Considering the accuracy and conveniency of density functional theory (DFT) methods, B3LYP function on the basis set of 6-31G(d,p) was employed in this letter to do calculations. The procedures are as follows. The molecular geometries were optimized, firstly, by molecular mechanic method, and then, by semiempirical quantum chemical method AM1. Finally, B3LYP/6-31G(d,p) was used for the full geometry optimization. The zero point vibrational energy (ZPVE) was scaled by a factor of 0.9805. The quantum chemical calculations were accomplished by Gaussian 94.

According to the method proposed by Wright and co-workers[11], the total energies, ZPVEs, and thermal corrections to energies for two comformations (**Scheme 1**) of parent catechols and corresponding radicals were calculated to estimate the H_{IHB}.

Scheme 1



Results and Discussion

The B3LYP/6-31G(d,p) calculated H_{IHB}, O-H charge differences, O-H bond lengths and bond orders for substituted catechols and their radicals are listed in **Table 1**. It can be seen that the H_{IHB} for catecholic radicals are roughly 20 kJ/mol higher than those for parent catechols, in good agreement with previous theoretical studies and the thermal decomposition study. Considering the accuracy of DFT methods in calculating short range forces, the H_{IHB} estimated by EPR equilibration technique is questionable. In fact, EPR equilibration technique is not appropriate to determine O-H BDEs for intramolecular hydrogen bonded molecules. A detailed investigation on this subject will be published elsewhere.

As IHB is dominated by electrostatic force, H_{IHB} is mainly determined by two factors. First is the charge difference between hydrogen bonded H and O. Apparently, the higher the charge difference, the stronger the IHB. Second is the bond length of IHB. It is easy to understand the shorter the bond length, the stronger the bond. As shown in **Table 1**, there really exists certain correlationship between H_{IHB} of catechols and O-H charge differences (r = 0.92799). The positive coefficient indicates that high charge difference is beneficial to strengthen the IHB. A similar correlation can be found between H_{IHB} of catecholic radicals and charge differences (r = 0.95939). Furthermore, the variation of the atom charge is determined by the substituents. Electron-donating groups will increase the O charge, and thus will strengthen the IHB, while electron-withdrawing groups have an opposite effect.

Table 1 B3LYP/6-31G(d,p) calculated H_{IHB} (× 4.184 kJ/mol), O-H charge differences (CD), O-H bond lengths (BL, angstrom) and O-H bond orders (BR) for parent catechols and corresponding radicals

X	$H_{\mathrm{IHB}}{}^{a}$	$H_{\mathrm{IHB}}{}^{b}$	O-H CD^{a}	O-H CD^{b}	O-H BL^{a}	O-H BL^{b}	O-H BR^{a}	O-H BR^{b}
H	4.09	9.58	0.928678	0.869466	2.123660	1.974376	0.020925	0.058169
Me	4.10	9.72	0.930479	0.874463	2.122483	1.973972	0.020957	0.058586
F	4.79	9.76	0.933701	0.871112	2.116488	1.974722	0.021420	0.057758
Cl	4.06	9.48	0.929728	0.867614	2.123703	1.981517	0.020875	0.056869
OH	4.88	10.70	0.937508	0.882480	2.120715	1.958679	0.021489	0.060721
OMe	4.76	10.69	0.936752	0.885500	2.122851	1.954607	0.021301	0.061445
SH	4.41	10.13	0.931856	0.876402	2.125315	1.970487	0.020985	0.058778
SMe	3.92	10.45	0.932422	0.881944	2.128012	1.964351	0.020901	0.060054
NH_2	4.54	10.74	0.937834	0.891358	2.117793	1.949823	0.021718	0.062278
NMe_2	4.49	10.82	0.936303	0.897094	2.130481	1.948788	0.020924	0.062909
CHO	3.02	8.38	0.918584	0.857604	2.123579	1.988759	0.020135	0.054838
CN	3.68	9.01	0.922918	0.858925	2.129346	1.992282	0.020099	0.054624
NO_2	3.27	8.41	0.920298	0.856225	2.130011	1.993144	0.019913	0.054382
CF_3	3.26	8.94	0.925387	0.863869	2.127983	1.986237	0.020375	0.056156

[a] data for parent catechols. [b] data for catecholic radicals.

It is also interesting to note that although the O-H charge differences for catechols are systematically higher than those for catecholic radicals, the bond strength of the former was lower than that of the latter, which results from the fact that H_{IHB} is also determined by O-H bond length. From **Table 1**, we can see the O-H bond lengths for catecholic radicals are systematically shorter than those for catechols, which may induce the H_{IHB} for the former systematically higher than that for the latter. So, it seems the H_{IHB} more sensitively depends on bond length rather than on charge difference. As to why the bond lengths are so different for catechols and their radicals, it also can be elucidated as follows. Theoretically speaking, the oxygen-centered radical has great tendency to form a chemical bond with the H atom. In fact, the bond orders for the IHB in catecholic radicals are much higher than those in catechols (**Table 1**), which will induce the bond length in catecholic radical getting shorter than that in parent catechol.

In summary, although the charge difference between hydrogen-bonded H and O plays a role in determining H_{IHB} for catechols and their radicals, H_{IHB} are mainly governed by the hydrogen bond length. Due to the shorter bond lengths in catecholic radicals than in catechols, the H_{IHB} for the former are systematically higher than those for the latter.

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