LETTER

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# A CCSD estimation of the O–H bond dissociation enthalpies of pyrogallol†‡

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**There is much debate on the homolytic O–H bond dissociation enthalpy (BDE) of pyrogallol. By means of a coupled-cluster method with single and double excitations at the 6-31+G* level, four BDEs corresponding to the three hydroxyl groups of pyrogallol were calculated, one of which supports the experimental value determined by time-resolved photoacoustic calorimetry. The other three are reported for the first time and are of significance to provide deeper insight into the H-atom donation behavior of pyrogallol.**

As a fundamental physico-chemical parameter, the homolytic bond dissociation enthalpy (BDE) has been broadly used in organic chemistry and medicinal chemistry.[1] For instance, the homolytic BDE has been successfully employed to characterize the radical-scavenging activity of antioxidants and to rationally design novel antioxidants.[2] Hence, considerable efforts, including experimental determinations[3–5] and theoretical calculations,[6] have been devoted to estimating homolytic BDEs of various compounds. The two approaches give consistent values in most cases, but there is some controversy over the O–H BDEs of intramolecularly hydrogen-bonded polyphenols, such as catechol and pyrogallol.[7–10] Although a consensus on the O–H BDE of catechol has been reached by combining an experimental determination,[7] theoretical calculations[8] and kinetic analysis,[9] the debate over the O–H BDE of pyrogallol remains open.

Using a hybrid density functional theory (DFT) method, labelled as (RO)B3LYP/6-311+G(2d,2p)//AM1/AM1, Wright *et al.* estimated the O–H BDE (BDE1, see Scheme 1) of pyrogallol (**1**) to be 14.1 kcal mol$^{-1}$ lower than that of phenol.[11] Based on an EPR radical equilibration technique, Lucarini *et al.* determined the O–H BDEs of propyl gallate (**2**) and octyl gallate (**3**, see Scheme 2) to be 81.2 kcal mol$^{-1}$, from which a much higher value of BDE1 (7.9 kcal mol$^{-1}$ lower than that of phenol) was derived through group-additivity analysis.[10] The important difference between the theoretical calculation and the experimental determination was compromised by recent studies. Through DFT calculations using B3LYP/6-31+G(,3pd) and CBS-4M methods, Bakalbassis *et al.*[8a] and Correia *et al.*[7] provided relative BDE1s of −11.29 and −12.7 kcal mol$^{-1}$, respectively (absolute value: 77.40 kcal mol$^{-1}$). In addition, by means of time-resolved photoacoustic calorimetry, Correia *et al.*[7] proposed a relative value of −10.5 kcal mol$^{-1}$ (absolute value at 298 K : 78.6 kcal mol$^{-1}$). Therefore, one must concede that more efforts are required to propose a consistent BDE1 of the O–H bond in pyrogallol. Moreover, as illustrated in Scheme 1, there exist three other O–H BDEs (BDE2, BDE3 and BDE4) for pyrogallol, for which no information has been obtained.

In order to get some insights into BDE2–4 and to evaluate the existing BDE1 of pyrogallol, we attempted to calculate the four BDEs by a coupled-cluster method with single and double excitations (CCSD), which has been successfully used to calculate the O–H BDE of catechol, an intramolecular hydrogen-bonded phenol.[8b]

Although pyrogallol can exist in two conformations (Scheme 3), **1** is more stable than **4**, because of the presence of double intramolecular hydrogen bonds (IHBs). Hence, **1** was employed as the starting point to calculate the O–H BDEs.

As indicated in Scheme 1, the BDE1 of pyrogallol is calculated to be 77.12 kcal mol$^{-1}$, 10.48 kcal mol$^{-1}$ lower than that of phenol, which is in excellent agreement with the experimental value given by Correia *et al.* (−10.5 kcal mol$^{-1}$).[7,12] Since time-resolved photoacoustic calorimetry also reliably gave the O–H BDE of catechol,[7] it is reasonable to consider that the (RO)B3LYP/6-311+G(2d,2p)//AM1/AM1 method underestimated the BDE1, while the EPR radical equilibration technique overestimated it by several kcal mol$^{-1}$. Similarly, an under- or overestimation by both methods of the O–H BDE of catechol was indicated in previous studies.[9] According to the error analyses of both methods, the underestimation by the DFT method of BDE1 is more likely to result from an overestimation of the IHB energy,[8b] while the overestimation by the EPR technique of BDE1 partially arises from the invalidity of group additivity.[13]

The group-additivity analysis is a convenient method to estimate O–H BDEs of monophenols. But the group-additivity analysis becomes complicated for intramolecularly hydrogen-bonded polyphenols.[13] According to its definition, the group-additivity concept is valid for intramolecular hydrogen-bonded polyphenols only if the substituent groups exhibit similar effects on the IHB energies of polyphenols and the derived radicals thereof,[14] which means that the IHB in the parent molecule preserves its conformation after H-atom abstraction.[14] Although the COOR group displays similar effects on the IHB1 and IHB1′ energies, because of the identical orientation of both IHBs (Scheme 2), it exhibits distinct effects on the IHB2 and IHB2′ energies, due to their different directions (Scheme 2). That is, the COOR group is meta to the OH in position 1 and, thus, has little effect on the net charge of O1. As a result, IHB2 is only slightly influenced by COOR. In

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† Electronic supplementary information (ESI) available: optimized structures, total energies and thermal corrections to enthalpy for all calculated molecules. See http://www.rsc.org/suppdata/nj/b4/b416841k/

‡ Abbreviations: BDE, bond dissociation enthalpy; DFT, density functional theory; CCSD, coupled-cluster method with single and double excitations; TCE, thermal correction to enthalpy; IHB, intramolecular hydrogen bond.

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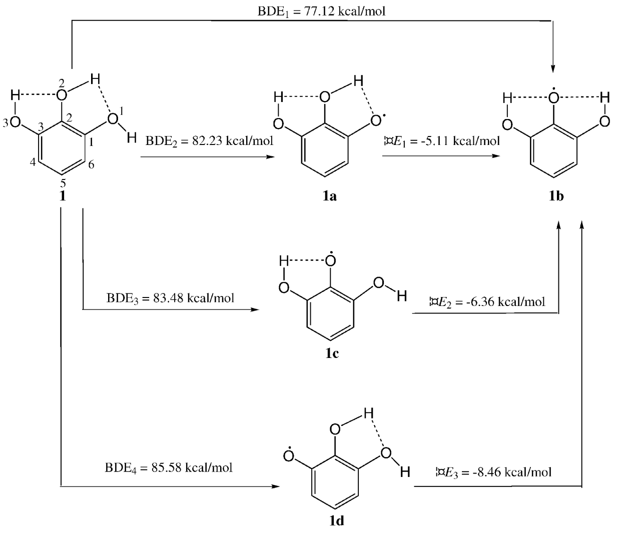
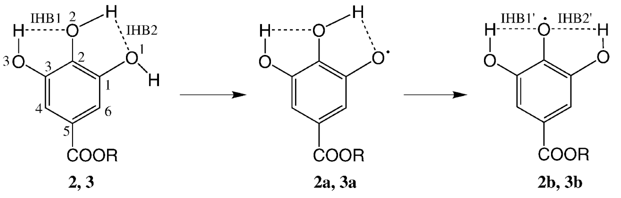


**Scheme 1** CCSD/6-31 + G* calculated O–H BDEs for pyrogallol.

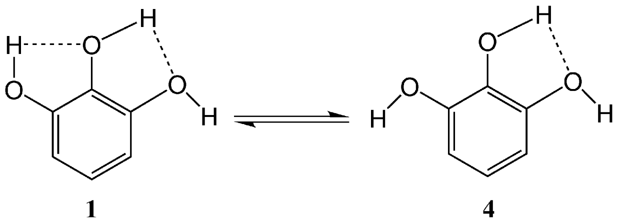
contrast, in **2b** and **3b**, the COOR group is para to the radical O$^{\bullet}$ in position 2, which decreases the net charge on O$^{\bullet}$ and, thus, weakens IHB2′. The distinct effects of COOR on IHB2 and IHB2′ invalidate the use of group additivity. As a consequence, it is disputable to use the substituent effect of COOR (1.5 kcal mol$^{-1}$) to deduce the O–H BDE of pyrogallol from the BDE between **2** and **2b**, and between **3** and **3b**.[10] In addition, another possible reason for the overestimation of BDE1 by the EPR technique may reside in the uncertainty of the method, as the O–H BDE of 3,5-di-*tert*-butylcatechol (79.4 kcal mol$^{-1}$), also determined in that study,[10] has been since updated as being equal to 78.2 kcal mol$^{-1}$ by a recent investigation.[8b]

The CCSD calculations also give BDE2–4, which reflect the reactivity of corresponding hydroxyls in the H-atom-abstraction reaction. It is interesting to note that BDE2 (82.23 kcal mol$^{-1}$) is slightly higher than the O–H BDE of catechol, calculated by the same method (81.6 kcal mol$^{-1}$),[8b] which must result from the electron-withdrawing effect of O(3)H.[15] The attenuated H-atom-donating ability of O(2)H and O(3)H can be explained by the fact that the related H-atom-abstraction reactions have to overcome the IHB in parent pyrogallol. Furthermore, a higher BDE4 compared to BDE3 can be understood from the different behaviors of OH groups at meta or ortho positions. That is, O(1)H and O(3)H are ortho to O(2)H and, thus, have an electron-donating effect towards O(2)H, while for O(3)H the electron-donating effect of O(2)H is partially offset by the electron-withdrawing effect of O(1)H. In addition, from the energy difference between **1b** and **1c**, one can estimate the IHB energy for one hydroxyl group in **1b** to be 6.36 kcal mol$^{-1}$, which is 1.64 kcal mol$^{-1}$ lower than that for the catecholic radical[8b] and can be attributed to the fact that O(2)$^{\bullet}$ is also shared by O(3)H in **1b**.

In conclusion, the CCSD-calculated BDE1 of pyrogallol provides solid evidence to support the experimental value determined by time-resolved photoacoustic calorimetry. In addition, other BDEs besides BDE1 for pyrogallol are obtained, which are of significance to obtain deeper insight into the H-atom-donating behavior of pyrogallol.



**Scheme 2** Structures of propyl gallate (**2**), octyl gallate (**3**) and their derived radicals.



**Scheme 3** The two conformations of pyrogallol.

## Methodology

The molecular geometries were optimized firstly by the semi-empirical quantum chemical method AM1,[16] then by the DFT method[17] at the B3LYP/6-31 + G* level and finally by the CCSD/6-31 + G* method.[18] During the CCSD calculation, the core electrons were held frozen in estimation of electron correlation, since their inclusion would not be expected to significantly influence the optimum geometries.[8b] Thus, the molecular enthalpy consists of the CCSD/6-31 + G* calculated total energy and the B3LYP/6-31 + G* derived thermal correction to enthalpy (TCE, scaled by a factor of 0.9804).[19] The BDEs of pyrogallol (ArOH) were calculated according to eqn. (1), issued from an isodesmic approach:[8b]

$$\mathrm{BDE(ArOH)} = \mathrm{BDE_{exp}(PhOH)} + [H_{\mathrm{calcd}}(\mathrm{ArO^{\bullet}}) - H_{\mathrm{calcd}}(\mathrm{ArOH})] - [H_{\mathrm{calcd}}(\mathrm{PhO^{\bullet}}) - H_{\mathrm{calcd}}(\mathrm{PhOH})] \quad (1)$$

BDE$_{\mathrm{exp}}$(PhOH) is the experimentally determined O–H BDE of phenol and equals 87.6 kcal mol$^{-1}$,[20] $H_{\mathrm{calcd}}$(ArO$^{\bullet}$) and $H_{\mathrm{calcd}}$(PhO$^{\bullet}$) are calculated enthalpies for pyrogallolic radical and phenolic radical, respectively, while $H_{\mathrm{calcd}}$(ArOH) and $H_{\mathrm{calcd}}$(PhOH) are calculated enthalpies for parent pyrogallol and phenol, respectively. The CCSD method and the isodesmic approach have been justified by a recent calculation on the O–H BDE of catechol.[8b] The CCSD/6-31G*, CCSD/6-31 + G* and CCSD/6-31 + + G** calculated O–H BDEs of catechol were 80.6, 81.6 and 81.5 kcal mol$^{-1}$, respectively,[8b] indicating that the basis set dependence of the CCSD method is rather weak, provided the diffuse function is included. Therefore, CCSD/6-31 + G* was employed in the present calculations. All of the calculations were accomplished with the Gaussian 03 program[21] on a SGI Origin 350 server with 8 CPUs.

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