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Theoretical Enthalpies of Formation and O−H Bond Dissociation Enthalpy of an Ubiquinol Model and Its Free Radical

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The standard enthalpies of formation of an ubiquinol model (where the isoprenoid units have been changed to a methyl group) and its free radical ubiquinoxy were estimated by DFT computations using isodesmic reactions as working chemical reactions and extended basis sets. In a first step, using aromatic compounds with experimentally well-established enthalpies of formation as test systems, the performance of the DFT functionals, the basis sets, and the working chemical reactions was analyzed. In a second step, the enthalpies of formation of other aromatic species also used as reference compounds in the thermochemical determination of ubiquinol and ubiquinoxy models were updated or calculated for the first time. The values for the 4-hydroxyphenoxy free radical and for 1,2-dimethoxybenzene were -31.6 ± 2.0 and -47.8 ± 2.0 kcal mol^{-1}, respectively, which are reported in this study for the first time. With this information, the recommended values for ubiquinol and ubiquinoxy models are, respectively, -147.0 ± 2.0 and -118.1 ± 2.0 kcal mol^{-1}. The error limits designate the estimated maximum uncertainties. These enthalpies of formation correspond to the O−H bond dissociation enthalpy of BDE(O−H) = 81.0 ± 2.0 kcal mol^{-1}, in excellent agreement with the only experimental value for natural ubiquinol, which lends confidence to the method and model used.

1. Introduction

Interest in the thermochemistry of ubiquinol (UQ-OH, the reduced form of coenzyme Q, CoQ) is due to the important role that it plays as an effective protection against free radical damage in biological systems and to the O−H bond being among the most frequently encountered in biochemistry. Natural radical-trapping antioxidants such as coenzyme Q (CoQ) and α-tocopherol (α-TOH, vitamin E), which partition in the lipid bilayer, can avoid, or at least significantly reduce, free radical reaction damage in a lipid environment.[1−4] As a result they afford efficient antioxidant protection to biological membranes[2,5,6] and to human low-density lipoproteins (LDL).[7−11] In living cells coenzyme Q functions also as an obligatory chemical intermediate electron carrier in the electron transport chains of mitochondria[12,13] and plasma membranes,[14] and it has been shown that NADH and ascorbic acid play major roles as electron donors for the reduction of oxidized coenzyme Q in mammalian cells.[14,15]

Surprisingly, despite its great importance in biochemistry, the enthalpies of formation of ubiquinol and its free radical have not been determined; while for the O−H bond dissociation enthalpy [BDE(O−H), 298.15 K], only one experimental and one theoretical measure have been reported.[16] These are from the work of Heer et al.[16] who give a value for ubiquinol-0 in gas-phase of BDE(O−H) = 78.5 ± 1.5 kcal mol^{-1}, using the photoacoustic calorimetry (PAC) experimental technique, and a value of 70.9 kcal mol^{-1} using the DFT/B3LYP method with the 6-31G(d,p) basis set, which is very far from their experimental result. This theoretical/experimental discrepancy was explained by the authors on the basis of previous studies,[17] which indicated that DFT calculations generally do not provide very accurate BDEs for bonds involving oxygen.

It is generally accepted that the best way of calculating theoretical enthalpy data is to use a thermochemical reaction (a "working chemical reaction") where computational errors (specifically, basis set effects) tend to cancel out. The more direct atomization approach usually gives far less accurate results. The choice of an isodesmic reaction, where the numbers of bonds and bond types are preserved on both sides of the reaction, is the preferred option whenever it can be applied.[18] The isogyric approach uses a working chemical reaction in which the number of electron pairs is left unchanged.[19] The accuracy of the enthalpies of formation obtained theoretically is conditioned by just a few factors: the level of sophistication (method + basis set) applied to calculate the electronic energy, the reliability of the enthalpies of formation of the reference compounds, the uncertainty in the thermal corrections, and very importantly, the choice of the working chemical reaction used in the evaluation. Sana et al.[20,21] carried out extensive studies on the requirements of accurately estimating theoretical enthalpies of formation for nonaromatic XYH_n species in connection with isogyric, X−Y hydrogenation, and hydrogen exchange reactions as working chemical reactions. They concluded that, on average, the enthalpies of formation of these nonaromatic species were underestimated when the isogyric approach was used and therefore recommended the two last reactions.

In the present work we report on a series of theoretical investigations aimed at establishing gas-phase enthalpies of formation for an ubiquinol (UQ-OH) model and its free radical (UQ-O) by various high-level density functional theory (DFT) methods. Isodesmic, bond hydrogenation, and hydrogen exchange reactions were applied to compute reaction enthalpies from which standard enthalpies of formation were derived. The computed enthalpies of formation will permit one to obtain the corresponding O−H bond dissociation enthalpy and to compare it with literature data.

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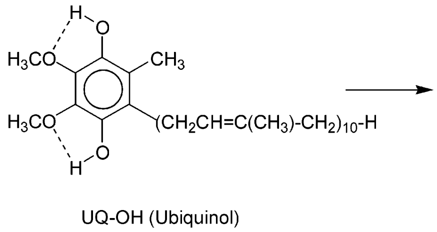
SCHEME 1



2. Methods and Computational Details

All calculations were carried out using the GAUSSIAN 98 system of programs.[22] The geometrical parameters were fully optimized by hybrid density functional theory (DFT) using two functionals: B3LYP,[23] which is based on Becke's three-parameter hybrid method (B3)[24] by combining Hartree−Fock exchange with the local density approximation exchange-correlation functional of Lee, Yang, and Parr (LYP),[25] and BHandHLYP, which is based on Becke's half-and-half method[26] and the LYP functional.[25] In both cases, the 6-31G basis set is used. For brevity, the levels used are denominated B3LYP/6-31G and BHandHLYP/6-31G, respectively, and they represent Level 0. Harmonic vibrational frequencies and zero-point vibrational energy (ZPE) were computed at these same levels of theory. The optimized geometrical parameters were used in five distinct theoretical single-point calculations (Levels I−V) using larger basis sets to obtain total electronic energies: Level I, B3LYP or BHandHLYP/6-31G(d,p); Level II, B3LYP or BHandHLYP/6-311+G(d,p); Level III, B3LYP or BHandHLYP/6-311G(2d,2p); Level IV, B3LYP or BHandHLYP/6-311+G(3df,2p); Level V, in this case, single-point calculations were performed at the B3LYP/ 6-311++G-(3d2f,3p) level, but now based on the geometries optimized at the B3LYP/6-31G(d,p) level. The shorthand notation for this computation is B3LYP/ 6-311++G(3d2f,3p)//B3LYP/6-31G-(d,p).

From the variety of DFT functionals in the bibliography, we chose the B3LYP functional because it is probably the most widely used functional in thermochemical calculations in the literature, and the BHandHLYP functional for comparisons. As will be seen in Results, the close agreement between the values obtained with these two functionals using different working chemical reactions, is an a posteriori justification for not applying other functionals in this work.

In natural ubiquinol the number of isoprenoid units can vary from six in some yeasts to 10 in humans.[27] Due to the large size of this molecular system, the real biological reaction has to be modeled. Foti et al.[28] found that the reaction of hydrogen abstraction from ubiquinol by phenoxyl radicals is independent of the number of isoprenoid units in the "tail", i.e., practically the same rate constants were found from 0 (ubiquinol-0) to 10 (ubiquinol-10) isoprenoid units. In the present work, the isoprenoid units in natural ubiquinol-10 were therefore changed to a methyl group (Scheme 1). Note that natural ubiquinol has two hydrogen bonds, between the OH and the methoxy group neighboring, which have been maintained in the model system.

3. Results and Discussion

3.1. Derivation of the Enthalpies of Formation. The standard enthalpies of formation of the molecule, UQ-OH, and its free radical, UQ-O, were estimated at each of the levels 0−IV from a consideration of applicable working chemical reactions where only the enthalpy of formation in question was unknown. The derivations were made according to the following procedure: (i) the total electronic energies for the reactants and the products were calculated, (ii) these were corrected for zero-point energies to obtain a theoretical reaction enthalpy at 0 K, (iii) thermal corrections were applied to get the reaction enthalpy at 298.15 K,; and (iv) this theoretical reaction enthalpy was combined with the known enthalpies of formation in the reaction (reference compounds) to solve for $\Delta H°_{f,298}$, the required enthalpy of formation at 298.15 K.

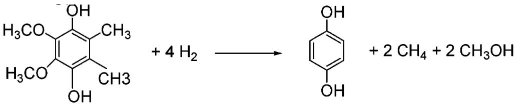
TABLE 1: Standard Enthalpies of Formation ($\Delta H°_{f,298}$), ZPE,[a] and TC[a] (298.15 K) (kcal mol^{-1})

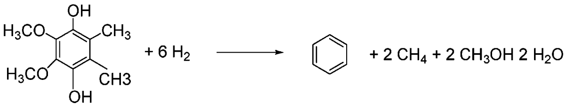
		B3LYP		BHandHLYP	
compound	$\Delta H°_{f,298}$	ZPE	TC	ZPE	TC
group i					
H	52.10[b]	0.0	1.48	0.0	1.48
H_2	0.0	6.60	1.48	6.52	1.48
H_2O	−57.80[b]	12.90	1.77	13.50	1.78
OH	9.40[b]	5.12	1.48	5.22	1.48
CH_4	−17.90[b]	28.55	1.79	29.40	1.80
CH_3OH	−48.18[c]	32.05	2.07	33.31	2.07
group ii					
benzene	19.74[c]	63.90	2.70	66.29	2.61
phenol	−23.03[c]	66.15	3.42	68.73	3.31
phenoxy	12.9 ± 1.4[d]	58.23	3.21	60.29	3.10
toluene	12.0[c]	81.20	3.29	84.16	3.18
1,2diMeBe	4.5 ± 0.3[f]	99.07	4.15	102.59	4.49
group iii					
hydroquinone	−63.4[c] −66.2 ± 0.3[g]	68.28	4.20	71.02	4.10
methoxybenzene	−16.2 ± 0.3[h] −18.3 ± 0.2[c] −16.9[i]	84.24	4.35	87.48	4.21
group iv					
4-HPR[j]	?	60.73	3.89	62.96	3.78
1,2-diMeOB[k]	?	104.35	5.56	108.44	5.39
new values					
ubiquinol	?	144.16	9.84	149.83	9.00
ubiquinoxy	?	136.58	8.48	141.77	8.22

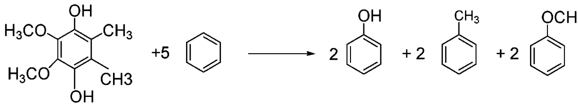
[a] ZPE and TC values obtained at level 0. [b] Reference 29. [c] Reference 30. [d] Reference 31. [e] 1,2-Dimethylbenzene. [f] Reference 32. [g] Reference 33. [h] Reference 34. [i] Reference 35. [j] 4-Hydroxyphenoxy radical. [k] 1,2-Dimethoxybenzene.

The zero-point energies (ZPE), the thermodynamic corrections (TC), and the standard enthalpies of formation of reference compounds are listed in Table 1. The thermal corrections were calculated with standard methods of statistical thermodynamics, $H°(T) - H°(0) = ZPE + TC = ZPE + \int_0^T CpdT$; and errors were compensated using the theoretical ZPEs and TCs calculated at level 0.

For the molecule, ubiquinol model UQ-OH, the following hydrogenation and isodesmic reactions were used as working chemical reactions in the study:


(R1)


(R2)


(R3)

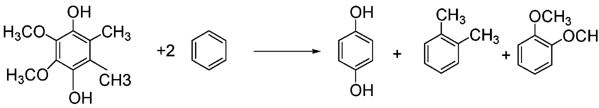
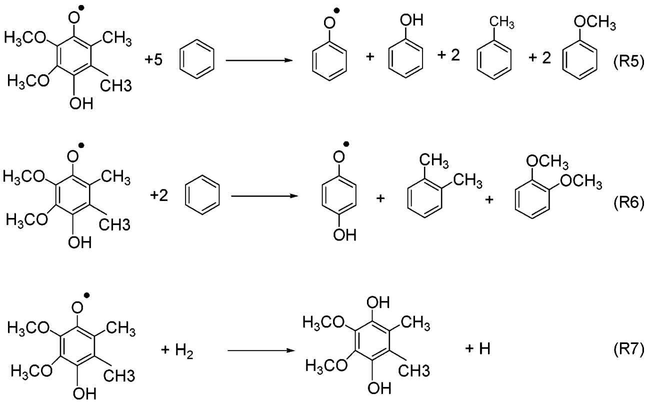

(R4)

TABLE 2: Computed Standard Enthalpies of Formation (298.15 K, 1 atm) for Phenol, Toluene, Phenoxy Radical, and 1,2-Dimethylbenzene at Several Levels and Functionals[a]

	phenol	toluene		phenoxy		1,2-dimethylbenzene		
level	(R8)	(R9)	(R10)	(R11)	(R12)	(R13)	(R14)	(R15)
0	−28.6/−25.0	14.3/15.2	19.8/17.2	4.4/5.5	19.9/23.5	9.4/8.9	11.7/12.0	7.2/5.7
I	−28.7/−26.2	13.0/13.9	18.7/17.0	7.1/8.0	16.2/20.3	8.2/7.7	9.8/9.5	7.2/5.8
II	−22.0/−21.0	14.2/14.6	13.3/12.4	8.0/8.7	14.6/18.1	9.4/9.0	11.6/11.2	7.2/5.9
III	−25.9/−23.8	14.3/14.8	17.3/15.6	9.6/10.2	16.1/20.0	9.6/8.7	12.0/11.5	7.3/5.9
IV	−22.9/−22.0	14.5/14.5	14.4/13.4	9.9/10.7	14.5/18.9	9.1/8.4	11.5/11.0	6.6/5.9
V	−23.0/	14.2/	14.3/	9.3/	14.0/	8.2/	10.5/	5.5/
exptl	−23.0 ± 0.1[b]	12.0 ± 0.1[b]		12.9 ± 1.4[c]		4.5 ± 0.3[d]		

[a] For each level the first entry corresponds to the B3LYP functional and the second to the BHandHLYP functional. Values in kcal mol^{-1}. [b] Reference 30. [c] Reference 31. [d] Reference 32.

For the free radical model, UQ-O, the following isodesmic and exchange reactions were used:



3.2. Reference Compounds. Usually, in thermochemistry calculations, the enthalpies of formation of the reference compounds are experimentally well established, and hence their name. But with large aromatic compounds this is not always the case, so that in the present work the reference compounds were classified into four categories:

(i) Nonaromatic compounds with well-established standard enthalpies of formation (H, H_2, H_2O, OH, CH_4, CH_3OH).

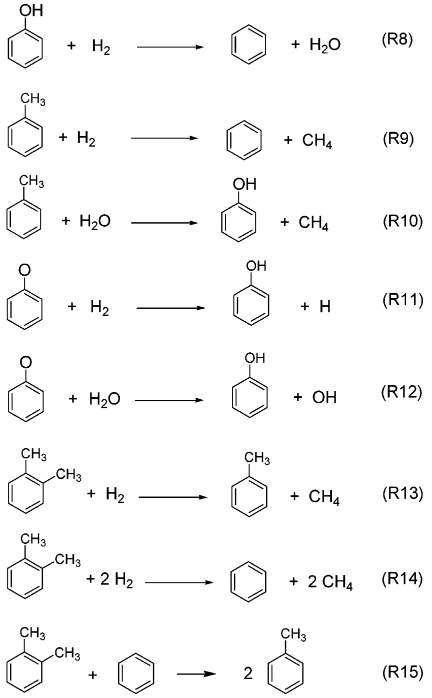
(ii) Aromatic compounds with well-established enthalpies of formation (benzene, phenol, toluene, phenoxy radical, 1,2-dimethylbenzene).

(iii) Aromatic compounds with experimental discrepancies in the standard enthalpies of formation (hydroquinone, methoxybenzene).

(iv) Aromatic compounds without experimental data (1,2-dimethoxybenzene, 4-hydroxyphenoxy radical).

With the main objective of assessing the performance of the basis set, the DFT functional, and the working chemical reaction in the calculations, we used the reference compounds of group ii in Table 1 as test molecules, because their standard enthalpies of formation are experimentally well-determined. The observations made with these molecules are believed to be transferrable also to the subsequent studies.

The following hydrogenation, exchange, and isodesmic reactions were used as working chemical reactions to obtain the $\Delta H°_{f,298}$ of phenol, toluene, phenoxy radical, and 1,2-dimethylbenzene, and the results of the theoretical computations at levels 0−V are summarized in Table 2.



In this case, it is necessary to differentiate between molecules and free radicals. For the molecules, first, levels II, IV, and V (which contain diffuse functions) gave the best agreement with the experimental data. Second, for these three levels, the agreement between the two functionals, B3LYP and BHandHLYP, was excellent (differences ≤1 kcal mol^{-1}). For the free radical, there were large differences according to which a working chemical reaction was used. While the (R11) reaction underestimated the experimental data, the (R12) reaction overestimated it. Both reactions are strongly dependent on the level of calculation, and only when high levels were used was any relative agreement with experiment found. Note that the (R12) reaction is more dependent on the functional used. Third, in all cases the difference between the results with levels IV and V was very small (≤1 kcal mol^{-1}) for each working chemical reaction, which justifies the use of the computationally more economical level IV in the rest of the study with larger molecular systems. Finally, for the 1,2-dimethylbenzene case, the isodesmic (R15) reaction was less dependent on the basis set and the functional than the hydrogenation (R13) and (R14) reactions and closer to the experimental data. This result advises against the use of hydrogenation reactions when isodesmic reactions with benzene are possible. This point will be returned to below. Therefore, using the reactions (R8), (R9), (R10), (R11), and (R15), the maximum estimated error for the B3LYP and BHandHLYP functionals at levels IV and V was ±2.5 kcal mol^{-1}, with an average error of ±2.0 kcal mol^{-1}, which will be the assumed error for these functionals in the rest of the paper.

With respect to the two reference compounds of group iii in Table 1, the reported experimental standard enthalpies of formation differ between different laboratories. The following hydrogenation, exchange, and isodesmic reactions, (R16)−

TABLE 3: Computed Standard Enthalpies of Formation (298.15 K, 1 atm) for Hydroquinone and Methoxybenzene at Several Levels and Functionals[a]

	hydroquinone			methoxybenzene	
level	(R16)	(R17)	(R18)	(R19)	(R20)
0	−70.0/−66.4	−75.5/−68.5	−64.4/−64.4	−19.1/−16.2	−13.6/−14.2
I	−69.8/−67.2	−75.5/−70.4	−64.1/−64.0	−19.4/−17.2	−13.7/−14.0
II	−63.2/−62.2	−62.3/−61.3	−64.1/−64.0	−14.2/−13.8	−14.8/−15.0
III	−66.8/−64.8	−69.8/−65.6	−63.8/−63.9	−16.1/−14.9	−13.4/−14.0
IV	−63.9/−62.8	−63.8/−61.7	−64.0/−63.4	−14.8/−14.1	−14.9/−15.1
exptl	−64.4;[b] −66.2 ± 0.3[c]			−16.2 ± 0.3;[d] −16.9;[e] −18.3 ± 0.2[b]	

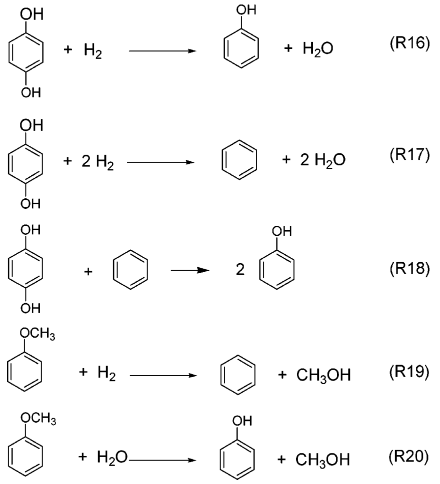
[a] B3LYP/BHandHLYP values in kcal mol^{-1}. [b] Reference 30. [c] Reference 33. [d] Reference 34. [e] Reference 35.

TABLE 4: Computed Standard Enthalpies of Formation (298.15 K, 1 atm) for 4-Hydroxyphenoxy Radical and 1,2-Dimethoxybenzene at Several Levels and Functionals[a]

	4-hydroxyphenoxy			1,2-dimethoxybenzene		
level	(R21)	(R22)	(R23)	(R24)	(R25)	(R26)
0	−37.2/−32.9	−35.7/−24.2	−31.7/−30.8	−51.3/−48.8	−54.2/−48.8	−48.3/−48.8
I	−37.7/−34.4	−40.1/−30.3	−32.0/−31.1	−50.8/−49.1	−54.0/−50.1	−47.6/−48.0
II	−31.1/−30.0	−28.5/−21.2	−32.0/−31.1	−45.8/−45.3	−43.8/−42.5	−47.9/−48.3
III	−35.0/−32.0	−34.7/−25.7	−32.0/−31.1	−47.6/−46.7	−47.5/−45.4	−47.6/−48.1
IV	−32.1/−30.2	−30.3/−23.0	−32.1/−31.2	−46.0/−44.3	−44.6/−43.4	−47.3/−47.7

[a] B3LYP/BHandHLYP values in kcal mol^{-1}. For methoxybenzene, the value $\Delta H°_{f,298} = -16.2 \pm 0.3$ was used.

(R20), were used as working chemical reactions to obtain the corresponding $\Delta H°_{f,298}$, and the results of the theoretical computations at levels 0-IV are summarized in Table 3.

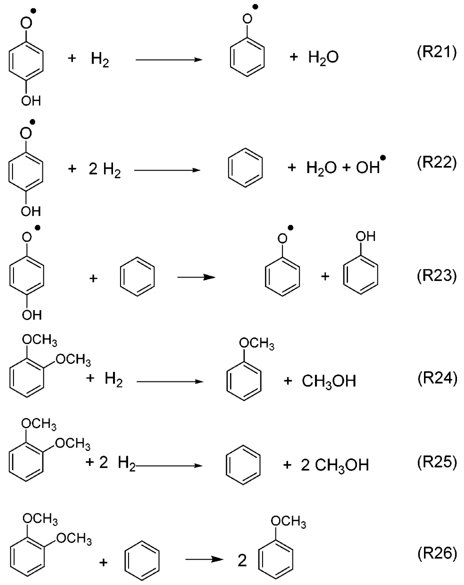


For hydroquinone, the results using the isodesmic (R18) reaction were practically independent of the basis set and the DFT functional used. The hydrogenation reactions (R16) and (R17), however, strongly depended on these two factors, and the first results were only reproduced when the largest basis sets (levels II and IV) were used. The close agreement between the predictions based on the various basis sets and functionals using the isodesmic reaction (R18) lends confidence to the unweighted average value that is recommended from levels II and IV, $\Delta H°_{f,298} = -64.0 \pm 0.1$ kcal mol^{-1}, where the quoted error limit is a single standard deviation. This value is intermediate between the two experimental determinations[30,33] and agrees with them within the precision of the present study, ±2.0 kcal mol^{-1}, and of experiment, ±0.3 kcal mol^{-1}.

For methoxybenzene, the reaction with benzene is not possible, and the hydrogenation (R19) and exchange (R20) reactions were used. In view of the conclusions obtained for the reference compounds of group ii and hydroquinone, levels II and IV were chosen because they perform better; i.e., they are less dependent on the functional and the working chemical reaction used. Note that the exchange reaction (R20) is less dependent on the DFT functional used than the X−Y hydrogenation reaction (R19). The close agreement between the predictions based on levels II and IV and the (R20) reaction lends confidence to the unweighted average value, $\Delta H°_{f,298} = -15.0 \pm 0.2$ kcal mol^{-1}. This value differs by 1−3 kcal mol^{-1} from the experimental data, suggesting that the lowest experimental value,[34] −16.2 ± 0.3, is the most accurate. To explore the accuracy of the proposed value, a calculation at level V was also performed for this molecule. The result, −15.1 kcal mol^{-1}, is also consistent with the average value, indicating the advisability of a review of the experimental results[30,34,35] for methoxybenzene's enthalpy of formation.

To close this section, let us analyze the two reference compounds of group iv in Table 1, for which experimental enthalpies of formation are unknown, and hence the values of the present study are the first to be reported. The following hydrogenation and isodesmic reactions, (R21)−(R26), were used as working chemical reactions to obtain the corresponding $\Delta H°_{f,298}$. The theoretical results at levels 0−IV are listed in Table 4. The hydrogenation reactions (R21), (R22), (R24), and (R25) were strongly dependent on the level of calculation, while the close agreement with the different levels for the isodesmic reactions (R23) and (R26) confirms the earlier conclusions about this type of reaction with aromatic compounds. Based on these reactions and the largest levels II and IV, the recommended unweighted averages for $\Delta H°_{f,298}$ are −31.6 ± 0.5 and −47.8 ± 0.4 kcal mol^{-1} for the 4-hydroxyphenoxy radical and 1,2-dimethoxybenzene, respectively, where the quoted error limit is a single standard deviation.

3.3. Standard Enthalpy of Formation of the Ubiquinol Model. The hydrogenation, (R1) and (R2), and the isodesmic, (R3) and (R4), reactions were used as working chemical reactions. Obviously, from the conclusions obtained for the reference compounds analyzed previously, the hydrogenation reactions were used only for comparative purposes. The standard enthalpies of formation determined theoretically for ubiquinol in the current work are listed in Table 5. From the isodesmic reactions, (R3) and (R4), using levels II and IV with the two functionals, we obtained an unweighted average value $\Delta H°_{f,298} = -147.0 \pm 1.5$ kcal mol^{-1}, where the quoted error limit is a single standard deviation. As already noted, the hydrogenation



reactions, (R1) and (R2), were strongly dependent on the level of calculation.

This recommended value is far from the average value obtained at levels II and IV using the hydrogenation (R1) and (R2) reactions: −135.1 ± 1.5 kcal mol^{-1}. This difference clearly indicates that in the hydrogenation reactions the effects of the benzene substituents on reactants and products are not conserved.

3.4. Standard Enthalpy of Formation of the Ubiquinoxy Radical Model. In these calculations the isodesmic reactions (R5) and (R6) and the hydrogenation reaction (R7) for comparison were applied in conjunction with the five levels 0−IV. The computed enthalpies of formation at 298 K are presented in Table 6. Once again, the proposed recommendation is the unweighted average of the data from the isodesmic reactions (R5) and (R6) at levels II and IV: −118.1 ± 1.5 kcal mol^{-1}, where the quoted error limit is a single standard deviation.

3.5. Discussion of the Enthalpy Results. First, the reference compounds of group ii (aromatic compounds with well-established standard enthalpies of formation) were used to assess the performance of the basis sets, the DFT functionals, and the working chemical reactions. The good agreement between levels II and IV (which include diffuse functions) for both DFT functionals, using the working chemical reactions (R8), (R9), (R10), (R11), and (R15), is reflected in an absolute average deviation of 2.0 kcal mol^{-1} from the mean values, which is the error assumed for these functionals in this work. The uncertainties arise from three sources: a substantial part from the calculation of the electronic energies using the two DFT functionals, to a lesser degree (tenths of kcalories per mole) from zero-point energy and thermal corrections, and finally from the error limits for the enthalpies of formation of the reference species, which were taken from their literature sources.

TABLE 5: Computed Standard Enthalpies of Formation (298.15 K, 1 atm) for Ubiquinol Model at Several Levels and Functionals[a]

level	(R1)	(R2)	(R3)	(R4)
0	−150.3/−144.4	−161.8/−149.5	−149.5/−151.8	−151.1/−151.6
I	−150.9/−146.6	−162.4/−153.6	−146.6/-149.0	−149.4/−149.9
II	−136.7/−135.0	−134.9/−131.8	−145.9/−147.2	−148.4/−148.9
III	−142.2/−139.8	−148.0/−142.0	−146.4/−148.7	−149.5/−149.8
IV	−136.7/−134.8	−136.6/−134.5	−144.5/−146.1	−147.0/−147.7

[a] B3LYP/BHandHLYP values in kcal mol^{-1}. For hydroquinone and 1,2-dimethoxybenzene, the $\Delta H°_{f,298}$ value from this work was used, −64.0 and −47.8 kcal/mol, respectively, and for methoxybenzene the value −16.2 ± 0.3 kcal/mol was used.

TABLE 6: Computed Standard Enthalpies of Formation (298.15 K, 1 atm) for Ubiquinoxy Radical Model at Several Levels and Functionals[a]

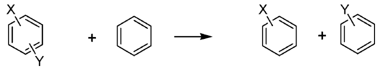
level	(R5)	(R6)	(R7)
0	−121.3/−119.8	−123.3/−120.8	−127.3/−122.4
I	−119.0/−117.8	−121.5/−119.3	−125.2/−120.7
II	−118.3/−117.0	−120.5/−118.5	−124.2/−120.1
III	−118.9/−117.7	−121.4/−119.3	−122.7/−119.3
IV	−117.5/−116.2	−119.4/−117.5	−123.0/−119.6

[a] B3LYP/BHandHLYP values in kcal mol^{-1}. For 4-hydroxyphenoxy, 1,2-dimethoxybenzene, and ubiquinol, the $\Delta H°_{f,298}$ value from this work was used, −31.6 ± 0.5, −47.8 ± 0.4, and −147.0 ± 1.5 kcal/mol, respectively, and for methoxybenzene the value −16.2 ± 0.3 kcal/mol was used.

Second, the reference compounds of group iii (aromatic compounds with experimental discrepancies in the standard enthalpy of formation) and group iv (aromatic compounds without experimental data) were analyzed. It was found that the working chemical reactions with benzene, (R15), (R18), (R23), and (R26), were isodesmic and depended little on the basis set and DFT functional used. Therefore, similar to the recommendation of the X−Y hydrogenation reactions

$$XYH_n + H_2 \rightarrow XH_p + YH_q$$

for nonaromatic compounds,[20,21] the conclusion of the present study is that isodesmic reactions with benzene or substituted benzenes are strongly recommended in thermochemical calculations of aromatic substituted compounds, whenever possible.



Clearly, in this reaction with benzene, the effects of the substituents on the reactants is maintained on the products, reflecting its isodesmic character.

The good agreement between the predicted enthalpies of formation at levels II and IV using the working chemical reactions (R18) for hydroquinone, (R20) for methoxybenzene, (R23) for 4-hydroxyphenoxy radical, and (R26) for 1,2-dimethoxybenzene lends confidence to those values and justifies the averaging. It should be noted that the enthalpies of formation of these two last species are reported in this study for the first time.

Third, for the ubiquinol and the ubiquinoxy radical models the isodesmic reactions, (R3)/(R4) and (R5)/(R6), were used at levels II and IV, respectively. Again, the good agreement between the predicted enthalpies of formation lends confidence to those values and justifies the averaging. The standard enthalpies of formation recommended from the present study are −147.0 ± 2.0 and −118.1 ± 2.0 kcal mol^{-1}, respectively, where the uncertainties were determined from the consideration of the possible sources of error. Table 7 summarizes the recommended values from this study, together with the experimentally determined enthalpies of formation for comparison.

Finally, the present theoretical enthalpies of formation given in Table 7 were used to calculate the O−H bond dissociation enthalpy at 298 K for ubiquinol, BDE(O−H) = 81.0 ± 2.0 kcal mol^{-1}. This value agrees with the only experimental determination,[16] 78.5 ± 1.5 kcal mol^{-1}, taking into account both uncertainties. Indirectly, this agreement lends confidence to

TABLE 7: Comparison of the Computed Enthalpies of Formation with Experiment (298.15 K, 1 atm), in kcal mol^{-1}

compound	$\Delta H°_{f,298}$/this work	$\Delta H°_{f,298}$/exptl	ref
hydroquinone	−64.0 ± 2.0	−63.4	30
		−66.2 ± 0.3	33
methoxybenzene	−15.0 ± 2.0	−16.2 ± 0.3	34
		−16.9	35
		−18.3 ± 0.2	30
4-hydroxyphenoxy	−31.6 ± 2.0		
1,2-dimethoxybenzene	−47.8 ± 2.0		
ubiquinol	−147.0 ± 2.0		
ubiquinoxy	−118.1 ± 2.0		

values proposed here for the enthalpies of formation of ubiquinol and ubiquinoxy and for the reference species used in determining them.

Conclusions

In this work we have reported for the first time the standard enthalpies of formation of an ubiquinol model (similar to ubiquinol-0) and its free radical ubiquinoxy, using two DFT functionals (B3LYP and BHandHLYP), extended basis sets, and isodesmic reactions as working chemical reactions.

First, using aromatic compounds with experimentally well-established enthalpies of formation as test systems, it was found that the B3LYP/DFT and BHandHLYP/DFT functionals show a similar behavior, that the inclusion of diffuse functions in the basis set is necessary to correctly describe the system, and that isodesmic reactions where benzene (or substituted benzene) is involved are preferred as working chemical reactions. Thus in thermochemical calculations of aromatic compounds we recommend this type of reaction as a working chemical reactions. Moreover, it was also found that the maximum estimated error for these two functionals with extended basis sets was ±2.5 kcal mol^{-1}, with an average error of ±2.0 kcal mol^{-1}.

Second, we estimated for the first time the standard enthalpies of formation of ubiquinol and ubiquinoxy models as the unweighted average of the data from the two DFT functionals using basis sets with diffuse functions and isodesmic reactions: −147.0 ± 2.0 and −118.1 ± 2.0 kcal mol^{-1}, respectively. In spite of the conclusions of Foti et al.[28] that the isoprenoid "tail" in natural ubiquinol has no influence on the kinetic results, we believe that the enthalpies of formation for the models used in this paper cannot be applied to natural ubiquinol and its free radical.

Finally, with these enthalpies of formation we found a value of 81.0 ± 2.0 kcal mol^{-1} for the O−H bond dissociation enthalpy, BDE(O−H). This value agrees with the only experimental value for natural ubiquinol, which indirectly lends confidence to the method and model used in this work. Moreover, this value is weaker than in unsubstituted phenol, 88.0 ± 1.5 kcal mol^{-1} (from the corresponding enthalpies of formation, Table 1), enhancing therefore its antioxidant role.

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