

STRUCTURE AND ANTIOXIDANT ABILITY OF FLAVONOIDS FROM LEAVES OF *PAEDERIA LANUGINOSA* FROM QUANGNAM, VIETNAM

CẤU TRÚC VÀ HOẠT TÍNH CHỐNG OXY HOÁ CỦA MỘT SỐ HỢP CHẤT FLAVONOID PHÂN LẬP TỪ LÁ CÂY MỜ LÔNG (*PAEDERIA LANUGINOSA*) THU HÁI TẠI QUẢNG NAM, VIỆT NAM

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Abstract - Three flavonoids (**FLVs**) were isolated from the EtOAC extract of leaves of *Paederia Lanuginosa*, including kaempferol (**KF**), quercetin (**QCT**), and quercitrin (**QCTR**). Their structures were analyzed and confirmed by the combination of the NMR spectroscopies and literature data. Their antioxidant activities were also examined *in-silico* in the aqueous solution at pH 7.4 by using the density functional theory. All three of **FLVs** were predicted to be good antioxidants in the polar environment, with $k_{overall}$ are 6.2×10^6 , 8.0×10^6 , and 1.4×10^6 , respectively. The main distribution into their capacity of antioxidant in the aqueous solution at pH 7.4 belongs to the dianion state, whereas the anion state does not make any distribution. The hydroxyl substitution at the O-3' site as well as the glycosidic linkage at the O-3 site of **KF** is almost not impacted its antioxidant ability.

Key words - Flavonoids; *Paederia Lanuginosa*; antioxidant; rate constant; single electron transfer

1. Introduction

Paederia Lanuginosa is a species of the Paderia genus of the Rubiaceae family, which is a widely used medicinal herb in Vietnam, China, India, and Japan for the treatment of a variety of conditions. Previous studies reported the bioactive constituent of extract from species of *Paederia* genus, such as flavonoid [1, 2], iridoid glucoside [3-6], anthraquinone [7-9], and volatile oils [10-12]. Especially, among them, flavonoids are secondary metabolism compounds that are also extensively found in a range of fruits, vegetables and other food crops, with plenty of bio-activity, including anti-inflammation, anti-aging, scavenging of reactive oxygen species, activation of antioxidant enzymes, inhibition of oxidases [13-15]. Numerous experiment research on evaluating the antioxidant activity of flavonoids has reported recently [16-19]. However, not many *in-silico* studies elucidate the relevance between flavonoid structure and their capacity activity.

In recent years, diverse studies on the antioxidant activity of natural compounds via computational approaches [20-25]. The mechanism pathway of radical scavenging reactions was modeled by investigating thermodynamic parameters and kinetic calculations. The previous study also indicated the main distribution of each pathway into the capacity of antioxidant in particular environments (gas phase, polar or non-polar solvent), such as the formal hydrogen transfer (FHT), single electron transfer followed

Tóm tắt - Từ dịch chiết EtOAC của lá cây Mờ lông (*Paederia Lanuginosa*) đã phân lập được ba hợp chất flavonoid, gồm kaempferol (**KF**), quercetin (**QCT**) và quercitrin (**QCTR**). Cấu trúc của các hợp chất này được xác định bằng các dữ liệu phổ NMR kết hợp với tài liệu tham khảo. Hoạt tính chống oxy hoá của các hợp chất trong môi trường nước (pH 7,4) cũng đã được đánh giá thông qua phương pháp tính toán hoá học. Kết quả cho thấy, cả ba hợp chất được phân lập thể hiện hoạt tính chống oxy hoá tốt với hằng số tốc độ phản ứng bất gộc tự do tổng quát lần lượt là $6,2 \times 10^6$, $8,0 \times 10^6$ và $1,4 \times 10^6$. Trạng thái dianion của các hợp chất trong môi trường nước (pH 7,4) là thành phần chính đóng góp vào khả năng bất gộc tự do của các hợp chất này, trong khi đó vai trò của trạng thái anion là không đáng kể. Bên cạnh đó, nhóm thế hydroxyl tại vị trí O-3' cũng như liên kết glycosidic tại vị trí O-3 của hợp chất KF không ảnh hưởng đến hoạt tính chống oxy hoá của các hợp chất nghiên cứu.

Từ khóa - Flavonoid; *Paederia Lanuginosa*; hoạt tính chống oxy hoá; hằng số tốc độ phản ứng; bước chuyển đơn điện tử

by proton transfer (SETPT), and sequential proton loss electron transfer (SPLET) [26-30]. The optimal computational method not only provides a realistic result but also saves time and resources in comparison with the experimental methods [31, 26, 32, 33].

This study focuses on confirming the structure of isolated flavonoids from the leaves of *Paederia Lanuginosa*, investigating the capacity and effect of structural characteristics on their antioxidant activity in aqueous solution, and comparing these findings to those of previous experiments.

2. Method

2.1. Extraction and isolation method

Powder of air-dried leaves of *Paederia Lanuginosa* (2.3 kg) was extracted three times by methanol. After the solvent was removed under vacuum, 1.5 L of distilled water was added to the concentrated extract and successive with n-hexane (1.5L-six times) and EtOAC (2.5L-three times). After the solvent removal using a rotary evaporator, the EtOAC extract then was subjected to Sephadex LH-20 column chromatography using CH_2Cl_2 : MeOH (1:1) to obtain eight fractions (E1-E8). Fraction 6 was subjected to RP-18 column chromatography eluted with gradient MeOH: Water (40:1-1:1) to give compounds LM8 (11.2 mg), LM9 (5.0 mg), LM10 (13.6 mg).

2.2. Structural analysis method

All the isolated compounds were characterized and identified by spectroscopic methods ($^1\text{H-NMR}$, $^{13}\text{C-NMR}$, ^1H , $^1\text{H-COSY}$, HMBC, HSQC) and comparison with published data.

The NMR spectra were recorded on the Bruker Advance 500 spectrometer using TMS as an internal reference.

2.3. Computational method

Prior research has demonstrated that the SET mechanism is the primary pathway for the HOO \cdot radical scavenging activity of phenolic compounds in the aqueous solution, whereas the FHT reaction contributes less to this activity [34-36]. Their antioxidant activity was enhanced by the deprotonation of the OH groups [37-39]. The deprotonation in water eliminates the activation energy of the first step (PL-proton loss), driving the reaction directly to the second step (SET). Thus, in this study, the molar fraction as well as the contribution of each deprotonated state to the overall reaction rate constant must be examined.

The proton affinity of OH groups (PA), pK_a and molar fraction were calculated following the literature according to eqn (1), (2), (4) and (5) [26].

$$PA_n = H(H_i\text{FLV}^{n-}) + H(\text{H}^+) - H(H_i\text{FLV}^{(n-1)-}) \quad (1)$$

Where $H(H_i\text{FLV}^{(n-1)-})$, $H(H_i\text{FLV}^{n-})$ are enthalpies of each deprotonation state.

$$pK_a^{\text{calc}} = m\Delta G_{AB}^o + C_o \quad (2)$$

$$\Delta G_{AB}^o = \Delta G_{H_i\text{FLV}^{n-}}^o - \Delta G_{H_i\text{FLV}^{(n-1)-}}^o \quad (3)$$

Where m and C_o are empirically fitted parameters [40].

$$f(\text{FLV}^{n-}) = \frac{1}{1 + \sum_{i=1}^n \beta_i [\text{H}^+]^i} \quad (4)$$

$$f(H_i\text{FLV}^{(n-1)-}) = \beta_i [\text{H}^+]^i f(\text{FLV}^{n-}) \quad (5)$$

Where:

$$\beta_i = 10^{\sum_{j=1}^i pK_a(n+1-j)} \quad (6)$$

The rate constant (k) was calculated using the conventional transition state theory (TST) and 1 M standard state at 298.15 K [41, 37, 42-47].

$$k = \sigma \kappa \frac{k_B T}{h} e^{-(\Delta G^\ddagger)/RT} \quad (7)$$

where σ is the reaction symmetry number [48, 49], k contains the tunneling corrections calculated using the Eckart barrier [50], k_B is the Boltzmann constant, h is the Planck constant, ΔG^\ddagger is the Gibbs free energy of activations.

For the reaction following the SET mechanism, the Marcus Theory is used to estimate the activation energy barrier *via* the free energy of reaction (ΔG_o^{ET}) and the nuclear reorganization energy (λ) [51-53]:

$$\Delta G_{ET}^\ddagger = \frac{\lambda}{4} \left(1 + \frac{\Delta G_o^{ET}}{\lambda} \right)^2 \quad (8)$$

$$\lambda \approx \Delta E_{ET} - \Delta G_o^{ET} \quad (9)$$

Where ΔE_{ET} is the nonadiabatic energy difference between reactants and vertical products.

A correction must be applied for the reaction rate constant which is close to the diffusion limit for yielding a

realistic result, following the Collins-Kimball theory, calculated at 298.15 K in solvents [54].

$$k_{app} = \frac{k_{TST} k_D}{k_{TST} + k_D} \quad (10)$$

Where the k_D is steady-state Smoluchowski rate constant for an irreversible bimolecular diffusion-controlled reaction [26, 55], k_{TST} is the thermal rate constant, obtained from TST calculation.

$$k_D = 4\pi R_{AB} D_{AB} N_A \quad (11)$$

Where, R_{AB} is the reaction distance, N_A is the Avogadro number, D_{AB} is the mutual diffusion coefficient of reactants A and B [54, 56], D_A or D_B is estimated using the Stoke-Einstein formulation [57, 58]:

$$D_{A \text{ or } B} = \frac{k_B T}{6\pi\eta a_{A \text{ or } B}} \quad (12)$$

$$D_{AB} = D_A + D_B \quad (13)$$

η is the viscosity of the solvent and a is the radius of the solute.

All calculations in this study were carried out with Gaussian16 suite of programs with M06-2X functional, which showed good performance in thermodynamics and kinetics calculations, especially in the physiological environments [59, 60, 34, 61]. Due to the large molecules (>70 atoms), the 6-31+G(d) level of theory was used for thermodynamic and kinetic calculation with acceptable accuracy, proven by the previous study [62, 63, 25]. The radical scavenging of Trolox also was calculated as the same method for comparison.

3. Results and discussion

3.1. Structure of isolated flavonoids

3.1.1. Kaempferol (KF)

Compound LM8 was obtained as the yellow powder. The ^1H NMR and ^{13}C NMR data (Table S1) indicated the presence of fifteen carbon atoms, including six methine groups, and nine quaternary carbon atoms, with the signal of the carbonyl group (C-4) at δ_C 175.9. The ^1H NMR also had the peak of four protons of AA'-XX' spin-interaction of aromatic ring, assigned to peaks at δ_H 6.93 (dd, $^3J_{H-H} = 9.0$, $^4J_{H-H} = 1.8$, H-2'/H-6') and δ_H 8.04 (dd, $^3J_{H-H} = 9.0$, $^4J_{H-H} = 1.8$ Hz, H-3'/H-5'), confirmed that the B ring had the substitution at C-4'. Two of the doublet signals at δ_H 6.19 (d, $^4J_{H-H} = 2.4$ Hz, H-6) and δ_H 6.44 (d, $^4J_{H-H} = 1.8$ Hz, H-8) proved the meta substitution of two moieties of ring A. From the above data and the literature [64], the structure of LM8 was elucidated as kaempferol.

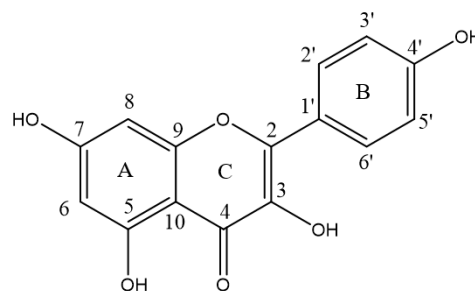


Figure 1. Structure of LM8

3.1.2. Quercitrin (QCTR)

Compound LM9 was obtained as the yellow powder. The ^1H NMR of compound LM9 (Table S2) showed three doublet peaks at δ_{H} 6.87 (1H, d, $^3J_{\text{H-H}} = 8.4$ Hz, H-5'), δ_{H} 7.25 (1H, dd, $^3J_{\text{H-H}} = 8.4$, $^4J_{\text{H-H}} = 2.4$ Hz, H-6') and δ_{H} 7.30 (1H, d, $^3J_{\text{H-H}} = 2.4$ Hz, H-2'), representing for protons at the 5'-, 6'- and 2'-position of aromatic ring B, respectively. Two resonances at δ_{H} 6.20 (1H, d, $^4J_{\text{H-H}} = 2.4$ Hz, H-6) và δ_{H} 6.39 (1H, d, $^4J_{\text{H-H}} = 2.4$ Hz, H-8) supported the presence of two protons located 6- and 8-position of aromatic ring A. According to this, the ^1H NMR data also has the signals of hydroxyl group at δ_{H} 12.65 (1H, s, H-5O), and methine group of sugar unit at δ_{H} 0.82 (3H, d, $^3J_{\text{H-H}} = 6.0$ Hz, H-6'').

The correlation between ^{13}C NMR and HSQC NMR elucidated that LM9 has twenty-one resonances, including fifteen carbon atoms corresponding to the number of carbon of flavonoid frame: one carbonyl carbon atom at δ_{C} 177.7 (C-4), six quaternary carbon atoms of A and C ring with chemical shifts at δ_{C} 156.4 (C-2), 134.2 (C-3), 161.3 (C-5), 164.1 (C-7), 157.2 (C-9), δ_{C} 104.0 (C-10), three quaternary carbon atoms of B ring at δ_{C} 120.7 (C-1'), 145.2 (C-3') and 148.4 (C-4'), five methyl carbon atoms of aromatic rings at 93.6 (C-8), 98.6 (C-6), 115.4 (C-2'), 115.6 (C-5') and 121.1 (C-6'), six carbon atoms of sugar unit at 17.4 (C-6''), 70.0 (C-5''), 70.3 (C-3''), 70.5 (C-2''), 71.1 (C-4''), and 101.8 (C-1''). Combination of ^1H -NMR and ^1H - ^1H COSY data showed that the signal of anomeric proton (H-1'') was located at δ_{H} 5.25 ppm. The data of 2D HMBC showed the interaction between anomeric proton of sugar unit (H-1'') and C-3 carbon of flavonoid frame, confirmed that the link of two moieties *via* oxygen bridge at C-3 carbon atom. Besides, the combination of the chemical shift of C-3'' (δ_{C} 70.3), C-5'' (δ_{C} 70.0), and anomeric proton H-1'' (δ_{H} 5.25) with the small coupling constant of 1.2 Hz indicated the configuration of methyl α -L-rhamnopyranose unit [65, 66]. Based on analyzed data, the structure of LM9 was known as quercitrin.

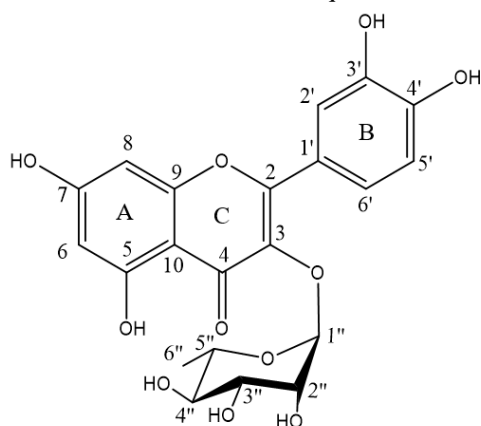


Figure 2. Structure of LM9

3.1.3. Quercetin (QCT)

Compound LM10 was isolated as a light-yellow powder. The ^1H NMR (Table S3) had two signals at δ_{H} 6.19 (d, $^4J_{\text{H-H}} = 1.8$ Hz) and δ_{H} 6.41 (d, $^4J_{\text{H-H}} = 1.8$ Hz), belonged to H-6 and H-8 meta proton of A ring, an ABX system at δ_{H} 6.89 (d, $^3J_{\text{H-H}} = 9.0$ Hz), 7.54 (dd, $^3J_{\text{H-H}} = 8.4$,

$^4J_{\text{H-H}} = 1.8$ Hz) and 7.68 (d, $^4J_{\text{H-H}} = 2.4$ Hz), corresponding to catechol proton of B ring. Besides, the resonances of two hydroxyl groups at δ_{H} 10.75 (s_{br} , 7-OH) and δ_{H} 12.45 (s, 5-OH) of A ring, a couple of broad-singlet of two hydroxyls of B ring at δ_{H} 9.27 (s, 3'-OH) and δ_{H} 9.32 (s, 4'-OH) were also revealed.

The ^{13}C NMR data showed the peaks of fifteen carbon atoms, including one of a carbonyl moiety at δ_{C} 175.8 (C-4), the characterized chemical shifts of flavone carbon atoms at δ_{C} 135.7 (C-3), 156.1 (C-5), 163.8 (C-7), 146.8 (C-3') and 147.7 (C-4'). Compare with the known literature [64], compound LM10 was determined as quercetin.

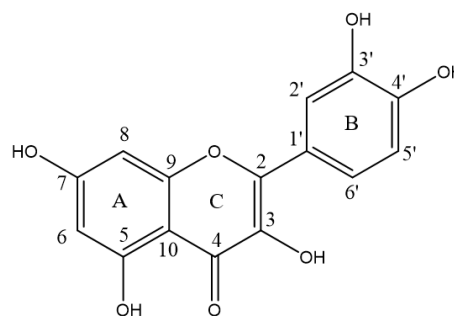


Figure 3. Structure of LM10

3.2. The HOO• radical scavenging of isolated flavonoids in water at pH 7.40

3.2.1. Acid-base equilibrium

The studied flavonoids have several OH moieties that can deprotonate. Thus, each substance should be assessed in the deprotonation order, *via* comparison of Gibbs free energies (ΔG , kcal mol $^{-1}$) of reaction corresponding to the different deprotonation positions. The pK_a values and the deprotonation order of **KF** and **QCT** were from the literature. The calculated ΔG values of each deprotonation stage of **QCTR** in water (pH = 7.4) of OH moieties are presented in Table 1. The pK_a values of each protonation stage are listed in Table 2.

Table 1. The calculated ΔG (kcal mol $^{-1}$) of **QCTR**

First deprotonation	Second deprotonation	Third deprotonation			
O-5	35.0	O-7-5	41.4	O-7-4'-3'	45.7
O-7	30.1	O-7-3'	36.3	O-7-4'-5	42.4
O-3'	35.6	O-7-4'	31.4	-	-
O-4'	30.4	-	-	-	-

Table 2. The pK_a values of the studied compounds

Comp.	pK_a	Positions	pK_a
KF	pK_{a1}	O-7	7.05 ^a
	pK_{a2}	O-4'	9.04 ^a
	pK_{a3}	O-5	11.04 ^a
QCT	pK_{a1}	O-7	7.19 ^a
	pK_{a2}	O-4'	9.36 ^a
	pK_{a3}	O-5	11.56 ^a
QCTR	pK_{a1}	O-7	7.45 ^b
	pK_{a2}	O-4'	7.88 ^b
	pK_{a3}	O-5	11.31 ^b

a: Ref [67]

b: Calculated in this work

The above data show that the deprotonation order of **QCTR** is 7, 4', and 5 site. This order is the same as that of **KF** and **QCT** reported by the previous study [67]. From the view of the structural difference between **KF**, **QCT** and **QCTR**, the hydroxyl substitution at O-3' site (**QCT**) as well as the glycosidic linkage at the O-3 site with l-rhamnopyranose (**QCTR**) increasing the pKa values but do not change the deprotonation order. The populations of each studied **FLVs** are shown in Figure 4.

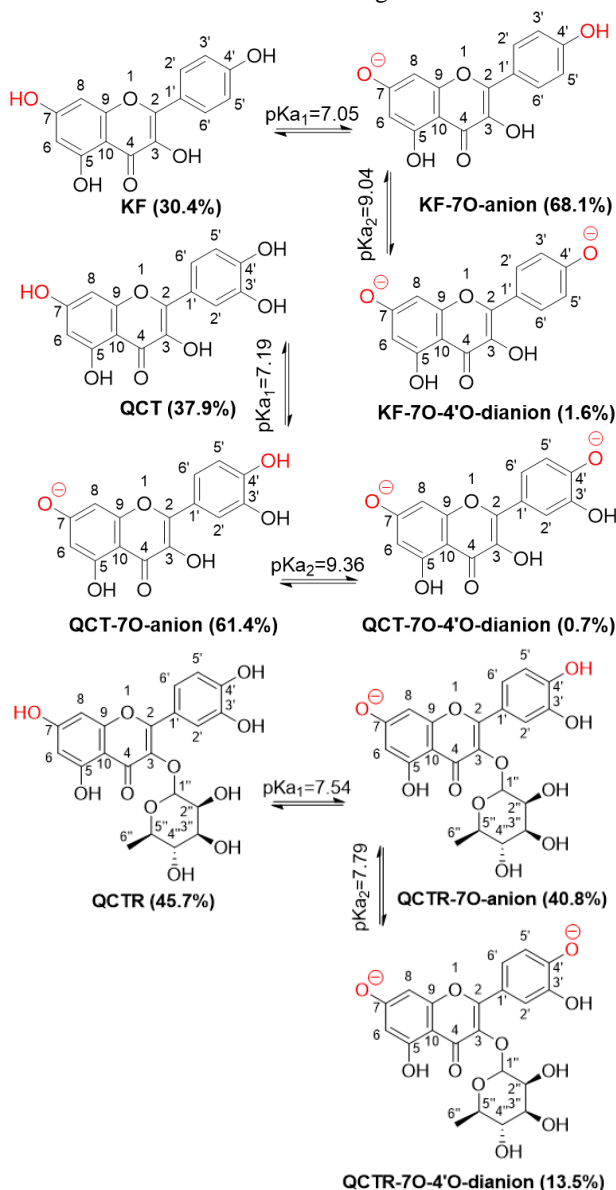


Figure 4. The deprotonation of studied substances in water at pH = 7.4

From the data of Table 2 and Figure 4, the pKa1, pKa2 and pKa3 of **KF** are 7.05, 9.04 and 11.04 respectively, at pH 7.4 yielding state populations of 30.4% of neutral, 68.1% of anion, and 1.6% of dianion. The pKa1, pKa2 and pKa3 of **QCT** are 7.19, 9.36 and 11.31, corresponding to 37.9% of neutral, 61.4% of anion, and 0.7% of dianion populations. The state proportions of **QCTR** are 45.7% of neutral, 40.8% of anion, and 13.5% of dianion (Figure 4). Thus, these populations were used for the kinetic calculation.

3.2.2. Kinetic of the HOO^\bullet radical scavenging reaction of studied substances in water (pH 7.40)

The overall reaction rate constant (k_{overall}) was calculated following the QM-ORSA protocol [37, 62], according to equations (13 and 14), and the results were listed in Table 7.

$$k_f = f \times k_{\text{app}} \quad (13)$$

$$k_{\text{overall}} = \sum k_f (\text{SET-neutral}) + \sum k_f (\text{SET-anion}) + \sum k_f (\text{SET-dianion}) \quad (14)$$

Table 3. Calculated activation Gibbs free energies ($\Delta G_{\text{ET}}^\ddagger$, kcal mol⁻¹), nuclear reorganization energy (λ , kcal mol⁻¹, k_{app} , k_f , k_{overall} (M⁻¹ s⁻¹) and branching ratios (Γ , %) for the HOO^\bullet scavenging of the **FLVs** in water following the SET pathway

Substance / Position	$\Delta G_{\text{ET}}^\ddagger$	λ	k_{app}	k_f	Γ	k_{overall}
KF	31.5	17.8	5.1×10^{-11}	1.5×10^{-11}	0.0	6.2×10^6
KF-7O-anion	18.1	14.1	3.6×10^{-1}	2.4×10^{-1}	0.0	–
KF-7O-4'O-dianion	5.7	12.1	4.0×10^8	6.2×10^6	100.0	–
QCT	29.9	17.9	7.7×10^{-10}	2.9×10^{-10}	0.0	8.0×10^6
QCT-7O-anion	18.3	14.0	2.2×10^{-1}	1.4×10^{-1}	0.0	–
QCT-7O-4'O-dianion	5.0	15.2	1.2×10^9	8.0×10^6	100.0	–
QCTR	38.0	16.9	9.0×10^{-16}	4.1×10^{-16}	0.0	1.4×10^6
QCTR-7O-anion	18.0	14.5	8.3×10^{-2}	3.4×10^{-2}	0.0	–
QCTR-7O-4'O-dianion	7.0	15.3	5.0×10^7	6.8×10^6	100.0	–
Trolox (f-anion ~100%)	11.3*	9.8**	3.0×10^5	–	–	3.0×10^5

* Activation Gibbs free energies for the HOO^\bullet scavenging of Trolox-anion in water following the FHT pathway;

** Eckart transmission coefficients.

As per calculated data, the k_{overall} of HOO^\bullet radical scavenging reaction of **KF**, **QCT** and **QCTR** are 6.2×10^6 , 8.0×10^6 , and 1.4×10^6 , respectively, nearly 5 to 27 times faster than that of reference Trolox ($k = 3.0 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$). The radical scavenging activity reactions of **FLVs** + HOO^\bullet are all dominated by the SET mechanism of dianion, with 100% of branching ratio, while the anion state does not make any distribution. The above data also show that, the hydroxyl substitution at the O-3' position (**QCT**) and the glycosidic linkage at the O-3 site with l-rhamnopyranose (**QCTR**) almost do not make any significant effects on antioxidant activities of studied **FLVs**.

Based on calculated data, It can be concluded that three studied **FLVs** are the good HOO^\bullet radical scavengers in the aqueous solution, better than that of Trolox ($k = 3.0 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$).

4. Conclusion

In this investigation, three FLVs were isolated and structurally confirmed using the NMR spectroscopy and comparison to reference data. The dianion states are primarily responsible for their effective HOO^\bullet radical scavenging activity at pH 7.4 in aqueous solution. The specific substitution at various sites of rings B and C of the investigated FLVs raises the pKa values of each protonation stage but does not affect the deprotonation order or the HOO^\bullet radical scavengers in an aqueous solution at physiological pH.

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REFERENCES

- N. Ishikura, Z. Yang, K. Yoshitama, and K. Kurosawa, "Flavonol glycosides from *Paederia scandens* var. *mairei*", *Zeitschrift für Naturforschung C*, vol. 45, no. 11, pp. 1081-1084, 1990.
- M. Chifumi, *et al.*, "Secondary Metabolites in the Leaves of *Paederia lanuginosa* Wall.", *the Japanese journal of pharmacognosy*, vol. 65, no. 1, pp. 52-53, 2011.
- D. H. He, J. S. Chen, X. L. Wang, and K. Y. Ding, "A new iridoid glycoside from *Paederia scandens*", *Chinese Chemical Letters*, vol. 21, no. 4, pp. 437-439, 2010.
- Y.-W. Chin, K.-D. Yoon, M. Ahn, and J.-W. Kim, "Two new phenylpropanoid glycosides from the aerial parts of *Paederia scandens*", *Bulletin of the Korean Chemical Society*, vol. 31, no. 4, pp. 1070-1072, 2010.
- Y. L. Kim, Y.-W. Chin, J. Kim, and J. H. Park, "Two new acylated iridoid glucosides from the aerial parts of *Paederia scandens*", *Chemical and pharmaceutical bulletin*, vol. 52, no. 11, pp. 1356-1357, 2004.
- X. Zou, S. Peng, X. Liu, B. Bai, and L. Ding, "Sulfur-containing iridoid glucosides from *Paederia scandens*", *Fitoterapia*, vol. 77, no. 5, pp. 374-377, 2006.
- D. N. Quang, "Anthraquinones from the roots of *Paederia scandens*", *Vietnam Journal of Chemistry*, vol. 47, no. 1, pp. 95-95, 2009.
- A. Ramadhan, A. K. Wardani, B. S. Dlamini, and C. Chang, "Anthraquinone derivatives and its antibacterial properties from *Paederia foetida* stems", *The Natural Products Journal*, vol. 11, no. 2, pp. 193-199, 2021.
- X. Zhang, H.-F. Zhou, M.-Y. Li, X.-Y. Yue, and T. Wu, "Three new anthraquinones from aerial parts of *Paederia scandens*", *Chemistry of Natural Compounds*, vol. 54, pp. 245-248, 2018.
- Y. Ainong, G. Fajun, and L. Dingshu, "Studies on the chemical constituents of the essential oil from fresh *Paederia scandens* (Lour.) Merr", *Journal of Hubei Institute for Nationalities (Natural Science)*, vol. 21, no. 1, pp. 41-43, 2003.
- K. Wong and GL Tan, "Steam volatile constituents of the aerial parts of *Paederia foetida* L", *Flavour and fragrance journal*, vol. 9, no. 1 pp. 25-28, 1994.
- K. Yang, Q. Z. Liu, Z. L. Liu, and S. S. Du, "GC-MS analysis of insecticidal essential oil of aerial parts of *Paederia scandens* (Lour) Merrill (Rubiaceae)", *Tropical Journal of Pharmaceutical Research*, vol. 11, no. 3, pp. 461-467, 2012.
- D. Gentile, *et al.*, "Dietary flavonoids as a potential intervention to improve redox balance in obesity and related co-morbidities: a review", *Nutrition research reviews*, vol. 31, no. 2, pp. 239-247, 2018.
- H. Guven, A. Arici, and O. Simsek, "Flavonoids in our foods: a short review", *Journal of Basic and Clinical Health Sciences*, vol. 3, pp. 96-106, 2019.
- W. He *et al.*, "Citrus aurantium L. and its flavonoids regulate TNBS-induced inflammatory bowel disease through anti-inflammation and suppressing isolated jejunum contraction", *International journal of molecular sciences*, vol. 19, no. 10, p. 3057, 2018.
- N. Andarwulan, R. Batari, D. A. Sandrasari, B. Bolling, and H. Wijaya, "Flavonoid content and antioxidant activity of vegetables from Indonesia", *Food chemistry*, vol. 121, no. 4, pp. 1231-1235, 2010.
- Y.-H. Chu, C.-L. Chang, and H.-F. Hsu, "Flavonoid content of several vegetables and their antioxidant activity", *Journal of the Science of Food and Agriculture*, vol. 80, no. 5, pp. 561-566, 2000.
- N. Shen *et al.*, "Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity", *Food Chemistry*, vol. 383, p. 132531, 2022.
- Z. Xiao *et al.*, "Relationships between structure and antioxidant capacity and activity of glycosylated flavonols", *Foods*, vol. 10, no. 4, p. 849, 2021.
- E. Alvareda, P. A. Denis, F. Iribarne, and M. Paulino, "Bond dissociation energies and enthalpies of formation of flavonoids: A G4 and M06-2X investigation", *Comput. Theor. Chem.*, vol. 1091, pp. 18-23, 2016.
- P. A Denis, "Coupled cluster, B2PLYP and M06-2X investigation of the thermochemistry of five-membered nitrogen containing heterocycles, furan, and thiophene", *Theor. Chem. Acc.*, vol. 129, no. 2, pp. 219-227, 2011.
- A. Galano, "Free radicals induced oxidative stress at a molecular level: The current status, challenges and perspectives of computational chemistry based protocols", *Journal of the Mexican Chemical Society*, vol. 59, pp. 231-262, 2015.
- A. Galano and J. R. Alvarez-Idaboy, "Computational strategies for predicting free radical scavengers' protection against oxidative stress: Where are we and what might follow?", *Int. J. Quantum Chem.*, vol. 119, no. 2, p. e25665, 2019.
- D. T. N. Hang, N. T. Hoa, H. N. Bich, A. Mechler, and Q. V. Vo, "The hydroperoxyl radical scavenging activity of natural hydroxybenzoic acids in oil and aqueous environments: Insights into the mechanism and kinetics", *Phytochemistry*, vol. 201, p. 113281, 2022.
- N. Q. Trung, A. Mechler, N. T. Hoa, and Q. V. Vo, "Calculating bond dissociation energies of X-H (X= C, N, O, S) bonds of aromatic systems via density functional theory: a detailed comparison of methods", *Royal Society Open Science*, vol. 9, p. 220177, 2022.
- A. Galano and J. R. Alvarez-Idaboy, "A computational methodology for accurate predictions of rate constants in solution: Application to the assessment of primary antioxidant activity", *Journal of computational chemistry*, vol. 34, no. 28, pp. 2430-2445, 2013.
- M. Leopoldini, N. Russo, and M. Toscano, "The molecular basis of working mechanism of natural polyphenolic antioxidants", *Food chemistry*, vol. 125, no. 2, pp. 288-306, 2011.
- N. Nenadis and M. Z Tsimidou, "Contribution of DFT computed molecular descriptors in the study of radical scavenging activity trend of natural hydroxybenzaldehydes and corresponding acids", *Food research international*, vol. 48, no. 2, pp. 538-543, 2012.
- N. M. Thong *et al.*, "Antioxidant properties of xanthenes extracted from the pericarp of *Garcinia mangostana* (Mangosteen): A theoretical study", *Chemical Physics Letters*, vol. 625, pp. 30-35, 2015.
- J S Wright I, E R Johnson, and G A DiLabio, "Predicting the activity of phenolic antioxidants: theoretical method, analysis of substituent effects, and application to major families of antioxidants", *Journal of the American Chemical Society*, vol. 123, no. 6, pp. 1173-1183, 2001.
- B. Alessandro, F. Rastrelli, and G. Saielli, "Toward the complete prediction of the 1H and 13C NMR spectra of complex organic molecules by DFT methods: application to natural substances", *Chemistry—A European Journal*, vol. 12, no. 21, pp. 5514-5525, 2006.
- A. Galano and J. R. Alvarez-Idaboy, "Computational strategies for predicting free radical scavengers' protection against oxidative stress: where are we and what might follow?", *International Journal of Quantum Chemistry*, vol. 119, no. 2, p. e25665, 2019.
- Q. V. Vo and A. Mechler, "In silico study of the radical scavenging activities of natural indole-3-carbinols", *Journal of Chemical Information and Modeling*, vol. 60, no. 1, pp. 316-321, 2019.
- A. Galano and J. R. Alvarez-Idaboy, "Kinetics of radical-molecule reactions in aqueous solution: A benchmark study of the performance of density functional methods", *Journal of computational chemistry*, vol. 35, no. 28, pp. 2019-2026, 2014.
- Q. V. Vo *et al.*, "A theoretical study of the radical scavenging activity of natural stilbenes", *RSC advances*, vol. 9, pp. 42020-42028, 2019.
- Q. V. Vo *et al.*, "A thermodynamic and kinetic study of the antioxidant activity of natural hydroanthraquinones", *RSC advances*, vol. 10, no. 34, pp. 20089-20097, 2020.
- E. Dzib *et al.*, "Eyringpy: A program for computing rate constants

- in the gas phase and in solution", *International Journal of Quantum Chemistry*, vol. 119, no. 2, p. e25686, 2019.
- [38] A. Galano and J. R. Alvarez-Idaboy, "Kinetics of radical-molecule reactions in aqueous solution: A benchmark study of the performance of density functional methods", *J. Comput. Chem.*, vol. 35, no. 28, pp. 2019-2026, 2014.
- [39] Q. V. Vo *et al.*, "Theoretical and Experimental Studies of the Antioxidant and Antinitrosant Activity of Syringic Acid", *J. Org. Chem.*, vol. 85, no. 23, pp. 15514-15520, 2020.
- [40] A. Galano *et al.*, "Empirically fitted parameters for calculating p K_a values with small deviations from experiments using a simple computational strategy", *Journal of Chemical Information and Modeling*, vol. 56, no. 9, pp. 1714-1724, 2016.
- [41] H. Boulebd, A. Mechler, N. T. Hoa, and Q. V. Vo, "Thermodynamic and kinetic studies of the antiradical activity of 5-hydroxymethylfurfural: computational insights", *New Journal of Chemistry*, no. 23, pp. 4-8, 2020.
- [42] E. Dzib, *et al.*, *Eyringpy 1.0.2*, 2018, Cinvestav, Mérida, Yucatán, 2018.
- [43] M. G. Evans and M. Polanyi, "Some applications of the transition state method to the calculation of reaction velocities, especially in solution", *Trans. Faraday Soc.*, vol. 31, pp. 875-894, 1935.
- [44] H. Eyring, "The Activated Complex in Chemical Reactions", *J. Chem. Phys.*, vol. 3, no. 2, pp. 107-115, 1935.
- [45] T. F. Özaltın, I U Gur, I. De, V. Aviyente, "Role of chain transfer agents in free radical polymerization kinetics", *Macromolecules*, vol. 43, pp. 1823-1835, 2010.
- [46] D. G. Truhlar, W. L. Hase and J. T. Hynes, "Current Status of Transition-State Theory", *J. Phys. Chem.*, vol. 87, no. 15, pp. 2664-2682, 1983.
- [47] E. Vélez *et al.*, "A computational study of stereospecificity in the thermal elimination reaction of menthyl benzoate in the gas phase", *J. Phys. Org. Chem.*, vol. 22, no. 10, pp. 971-977, 2009.
- [48] A. Fernández-Ramos *et al.*, "Symmetry numbers and chemical reaction rates", *Theor. Chem. Acc.*, vol. 118, pp. 813-826, 2007.
- [49] E. Pollak and P. Pechukas, "Symmetry numbers, not statistical factors, should be used in absolute rate theory and in Bronsted relations", *J. Am. Chem. Soc.*, vol. 100, no. 10, pp. 2984-2991, 1978.
- [50] C. Eckart, "The penetration of a potential barrier by electrons", *Phys. Rev.*, vol. 35, no. 11, p. 1303, 1930.
- [51] Y. Lu, A. Wang, P. Shi, H. Zhang, and Z. Li, "Quantum chemical study on the antioxidation mechanism of piceatannol and isorhapontigenin toward hydroxyl and hydroperoxyl radicals", *PLoS one*, vol. 10, p. e0133259, 2015.
- [52] R. A. Marcus, "Chemical and electrochemical electron-transfer theory", *Annual review of physical chemistry*, vol. 15, pp. 155-196, 1964.
- [53] R. A. Marcus, "Electron transfer reactions in chemistry. Theory and experiment", *Reviews of modern physics*, vol. 65, p. 599, 1993.
- [54] F. C. Collins and G. E. Kimball, "Diffusion-controlled reaction rates", *Journal of colloid science*, vol. 4, no. 4, pp. 425-437, 1949.
- [55] M. v. Smoluchowski, "Versuch einer mathematischen Theorie der Koagulationskinetik kolloider Lösungen", *Zeitschrift für physikalische Chemie*, vol. 92, pp. 129-168, 1918.
- [56] D. G. Truhlar, "Nearly encounter-controlled reactions: The equivalence of the steady-state and diffusional viewpoints", *Journal of Chemical Education*, vol. 62, no. 2, p. 104, 1985.
- [57] A. Einstein, "Veber die von der molekular theorethischen Theorie der Wärme geforderte Bewegung von in ruhenden Flüssigkeiten suspendierten Teilchen", *Ann. der Phys.(4)*, vol. 17, pp. 1904, 549.
- [58] G.G. Stokes, *reprinted in: Mathematical and Physical Papers*, vol. 5, Cambridge University Press, Cambridge, 1905.
- [59] H. Boulebd *et al.*, "Thermodynamic and kinetic studies of the radical scavenging behavior of hyalazine and dihyalazine: theoretical insights", *The Journal of Physical Chemistry B*, vol. 124, no. 20, pp. 4123-4131, 2020.
- [60] M. Carreon-Gonzalez, A. Vivier-Bunge, and J. R. Alvarez-Idaboy, "Thiophenols, promising scavengers of peroxy radicals: mechanisms and kinetics", *Journal of Computational Chemistry*, vol. 40, no. 24, pp. 2103-2110, 2019.
- [61] Y. Zhao and D. G. Truhlar, "How well can new-generation density functionals describe the energetics of bond-dissociation reactions producing radicals?", *The Journal of Physical Chemistry A*, vol. 112, no. 6, pp. 1095-1099, 2008.
- [62] A. Galano and J. R. Alvarez-Idaboy, "A computational methodology for accurate predictions of rate constants in solution: Application to the assessment of primary antioxidant activity", *J. Comput. Chem.*, vol. 34, no. 28, pp. 2430-2445, 2013.
- [63] M. Nowicki *et al.*, "DFT study of trialkylborohydride-catalysed hydrosilylation of alkenes—the mechanism and its implications", *Catal. Sci. Technol.*, vol. 10, no. 4, pp. 1066-1072, 2020.
- [64] L. Lin, X. Huang and Z. Lv, "Isolation and identification of flavonoids components from *Pteris vittata* L", *SpringerPlus*, vol. 5, pp. 1-3, 2016.
- [65] P. K. Agrawal, "NMR spectroscopy in the structural elucidation of oligosaccharides and glycosides", *Phytochemistry*, vol. 31, no. 10, pp. 3307-3330, 1992.
- [66] O. A. Eldahshan, "Isolation and structure elucidation of phenolic compounds of carob leaves grown in Egypt", *Curr Res J Biol Sci*, vol. 3, no. 1, pp. 52-55, 2011.
- [67] R. Álvarez-Diduk, M. T. Ramírez-Silva, A. Galano, and A. Merkoçi, "Deprotonation mechanism and acidity constants in aqueous solution of flavonols: a combined experimental and theoretical study", *The Journal of Physical Chemistry B*, vol. 117, no. 41, pp. 12347-12359, 2013.
- [68] M. E. Alberto *et al.*, "A physicochemical examination of the free radical scavenging activity of Trolox: mechanism, kinetics and influence of the environment", *Physical Chemistry Chemical Physics*, vol. 15, no. 13, pp. 4642-4650, 2013.
- [69] C. Iuga, J. R. Alvarez-Idaboy, and Russo, "Antioxidant activity of trans-resveratrol toward hydroxyl and hydroperoxyl radicals: a quantum chemical and computational kinetics study", *The Journal of organic chemistry*, vol. 77, no. 8, pp. 3868-3877, 2012.

SUPPORTING INFORMATION (SI)

Table S1. NMR spectra data of kaempferol (KF)

C	$\delta_C^{\#}$, ^a	$\delta_C^{\text{a,b}}$	$\delta_H^{\text{a,c}}$ (J, Hz)
2	146.8	146.8	–
3	135.6	135.6	–
4	175.9	175.9	–
5	156.2	156.1	–
6	98.2	98.2	6.19 (d, 2.4)
7	163.9	163.9	–
8	93.5	93.4	6.44 (d, 1.8)
9	160.7	160.7	–
10	103.0	103.0	–
1'	121.7	121.6	–
2'	129.5	129.5	6.93 (dd, 9.0, 1.8)
3'	115.4	115.4	8.04 (dd, 9.0, 1.8)
4'	159.2	159.2	–
5'	115.4	115.4	8.04 (dd, 9.0, 1.8)
6'	130.5	129.5	6.93 (dd, 9.0, 1.8)
3-OH	–	–	10.75 (br s)
5-OH	–	–	12.47 (s)
7-OH	–	–	10.08 (br s)
4'-OH	–	–	9.36 (br s)

[#] δ_C of kaempferol [64], ^ameasured in DMSO, ^b 125 MHz, ^c 600 MHz

Table S2. NMR spectra data of quercitrin (QCTR)

C	$\delta_C^{\#}$, ^a	$\delta_C^{\text{a,b}}$	$\delta_H^{\text{a,c}}$ (J, Hz)
2	156.7	156.4	–
3	134.2	134.2	–
4	177.7	177.7	–
5	161.4	161.3	–
6	99.2	98.6	6.20 (1H, d, 2.4)
7	165.6	164.1	–
8	94.0	93.6	6.39 (1H, d, 2.4)
9	157.3	157.2	–
10	103.8	104.0	–
1'	120.8	120.7	–

2'	115.7	115.4	7.30 (1H, d, 2.4)
3'	145.4	145.2	–
4'	148.8	148.4	–
5'	115.8	115.6	6.87 (1H, d, 8.4)
6'	121.2	121.1	7.25 (1H, dd, 8.4, 2.4)
1''	101.9	101.8	5.25 (1H, d, 1.2)
2''	70.5	70.5	3.99 (1H, br s)
3''	70.7	70.3	3.50 (1H, m)
4''	71.4	71.1	3.15 (1H, dd, 9.0, 4.2)
5''	70.2	70.0	3.22 (1H, m)
6''	17.7	17.4	0.82 (3H, d, 6.0)
5–OH	–	–	12.65 (1H, s)

[#] δ_c of quercitrin [65, 66], ^ameasured in DMSO, ^b 125 MHz, ^c 600 MHz

Table S3. NMR spectra data of quercerin (QCT)

C	$\delta_c^{\#}$, a	$\delta_c^{a,b}$	$\delta_H^{\#}$, c (J, Hz)
2	145.0	145.0	–
3	135.6	135.7	–
4	175.8	175.8	–
5	156.1	156.1	–
6	98.1	98.1	6.41 (d, 1.8)
7	163.8	163.8	–
8	93.3	93.3	6.19 (d, 1.8)
9	160.7	160.7	–
10	102.9	103.0	–
1'	121.8	121.9	–
2'	114.9	115.0	7.68 (d, 2.4)
3'	146.8	146.8	–
4'	147.6	147.7	–
5'	115.5	115.6	6.89 (d, 9.0)
6'	119.9	119.9	7.54 (dd, 8.4, 1.8)
3–OH	–	–	10.75 (br s)
5–OH	–	–	12.49 (s)
7–OH	–	–	9.56 (br s)
3'–OH	–	–	9.27 (br s)
4'–OH	–	–	9.32 (br s)

[#] δ_c of quercetin [64], ^ameasured in DMSO, ^b 125 MHz, ^c 600 MHz

Table S4. The Cartesian coordinates and energies of FLVs, ANION, DIANION in water

Name	KF			
Cartesian Coordinates	Energy			
O	-0.09380400	-0.79914700	-0.09439700	Zero-point correction=
O	0.85327000	2.68945800	0.16300300	0.227035
O	-4.20621900	1.67349300	0.09740800	(Hartree/Particle)
O	-1.81697100	2.86198700	0.16611500	Thermal correction to
O	-4.27931800	-3.02079400	-0.14166400	Energy= 0.243639
O	6.18137100	-0.89671800	-0.00732300	Thermal correction to
C	-2.10393400	0.50341000	0.00573500	Enthalpy= 0.244583
C	-1.44809600	-0.73473700	-0.07059400	Thermal correction to
C	0.68529900	0.31828900	-0.02656200	Gibbs Free Energy=
C	-1.32543000	1.70981600	0.07518200	0.182803
C	0.11289100	1.55003300	0.05720200	Sum of electronic and
C	2.11773000	0.00513300	-0.02524700	zero-point Energies=
C	-3.52448600	0.50607900	0.02436100	-1028.400907
C	-2.13447200	-1.94240900	-0.12631700	Sum of electronic and
C	-3.52515700	-1.89157200	-0.10097300	thermal Energies=
C	-4.22971700	-0.67979600	-0.02983800	-1028.384303
C	2.55460500	-1.24078000	0.45131500	Sum of electronic and
C	3.07105900	0.91940000	-0.50250500	thermal Enthalpies=
				-1028.383359
				Sum of electronic and

C	3.90522100	-1.56213300	0.46785200	thermal Free Energies=
C	4.42217500	0.60163900	-0.49319700	-1028.445139
C	4.84017800	-0.63676500	-0.00182000	
H	-1.59856100	-2.88427700	-0.18213400	
H	-5.31439700	-0.67817000	-0.01256700	
H	1.83413700	-1.96245400	0.82276600	
H	2.75699100	1.87719100	-0.90058200	
H	4.24113600	-2.52391600	0.84654400	
H	5.16077800	1.30321200	-0.86860700	
H	0.21527300	3.42438100	0.26673000	
H	-3.55257900	2.41139300	0.13925000	
H	-3.70830500	-3.80795800	-0.16833200	
H	6.35170800	-1.77925600	0.36422600	

Name	KF-7O-anion			
Cartesian Coordinates	Energy			
O	0.10829500	-0.82774500	0.09479700	Zero-point correction=
O	-0.78756500	2.67945300	-0.15474400	0.213864
O	4.25111400	1.61125700	-0.10717800	(Hartree/Particle)
O	1.87047600	2.82520300	-0.16868000	Thermal correction to
O	4.22293100	-3.11528200	0.16455100	Energy= 0.230284
O	-6.17208200	-0.84865400	0.00564300	Thermal correction to
C	2.13568600	0.46244600	-0.00995300	Enthalpy= 0.231228
C	1.47328200	-0.78450800	0.07069200	Thermal correction to
C	-0.65621600	0.30260200	0.02821700	Gibbs Free Energy=
C	1.37873500	1.66316700	-0.07615900	0.169566
C	-0.06794900	1.52281200	-0.05273900	Sum of electronic and
C	-2.09431200	0.00722000	0.02543600	zero-point Energies=
C	3.56292400	0.43549900	-0.02921400	-1027.954995
C	2.14089300	-1.98791800	0.13002300	Sum of electronic and
C	3.56941000	-2.01154200	0.11117800	thermal Energies=
C	4.25355700	-0.74812600	0.02940400	-1027.938574
C	-2.54726500	-1.23059400	-0.45638800	Sum of electronic and
C	-3.03779900	0.92922400	0.50650600	thermal Enthalpies=
C	-3.90209400	-1.53688500	-0.47361800	-1027.937630
C	-4.39332000	0.62764600	0.49569000	Sum of electronic and
C	-4.82619800	-0.60355500	0.00009800	thermal Free Energies=
H	1.58478400	-2.91800800	0.19120100	-1027.999292
H	5.33978800	-0.73931400	0.01314900	
H	-1.83529200	-1.95932800	-0.83044100	
H	-2.71241900	1.88169200	0.90873900	
H	-4.24851000	-2.49358900	-0.85589800	
H	-5.12343000	1.33647400	0.87435000	
H	-0.12748300	3.39608300	-0.25338200	
H	3.59300200	2.34499400	-0.14853800	
H	-6.35180100	-1.72780200	-0.36932800	

Name	KF-7O-4'O-dianion			
Cartesian Coordinates	Energy			
O	0.07226600	-0.82896300	0.08308400	Zero-point correction=
O	-0.83783900	2.67898300	-0.15363500	0.200666
O	4.20193100	1.62837300	-0.08285500	(Hartree/Particle)
O	1.82180300	2.83137100	-0.14737300	Thermal correction to
O	4.19698700	-3.10438700	0.14080400	Energy= 0.216804
O	-6.19293500	-0.95735400	-0.01828900	Thermal correction to
C	2.09349200	0.46769700	-0.00227400	Enthalpy= 0.217748
C	1.43693500	-0.78027300	0.06195500	Thermal correction to
C	-0.70590000	0.29486200	0.02112100	Gibbs Free Energy=
C	1.32544500	1.66620500	-0.06230600	0.156524
C	-0.11083000	1.52006300	-0.04818000	Sum of electronic and
C	-2.13132200	-0.00930600	0.01696100	zero-point Energies=
C	3.51867000	0.44757700	-0.01786100	-1027.502396
C	2.11005800	-1.98305600	0.10973300	Sum of electronic and
C	3.53755400	-2.00070700	0.09625500	thermal Energies=
C	4.21567800	-0.73434200	0.03041300	-1027.486259
C	-2.58395200	-1.27699100	-0.40601800	Sum of electronic and
C	-3.10217000	0.92077600	0.44261400	thermal Enthalpies=
C	-3.92928600	-1.59586000	-0.42041400	-1027.485315
C	-4.44955000	0.60581800	0.43670900	Sum of electronic and
				thermal Free Energies=

C	-4.93016900	-0.66569500	-0.00194100	-1027.546538
H	1.55708400	-2.91581700	0.15934300	
H	5.30197400	-0.71965400	0.01721300	
H	-1.86190000	-2.01766400	-0.73909700	
H	-2.79185700	1.89652400	0.80127100	
H	-4.25201500	-2.57701000	-0.76173500	
H	-5.17804000	1.33733000	0.77943000	
H	-0.17713000	3.39476300	-0.24911500	
H	3.53626400	2.35673200	-0.12179700	

Name	QCT			
Cartesian Coordinates	Energy			
O	-0.40894100	-0.86406300	0.05980100	Zero-point correction=
O	0.70106900	2.57184100	-0.25218600	0.230076
O	-4.39876000	1.80339200	-0.08734200	(Hartree/Particle)
O	-1.95388500	2.87358000	-0.21134500	Thermal correction to
O	-4.59896100	-2.93888300	0.26436100	Energy= 0.248231
O	5.22119600	1.12134100	0.66248100	Thermal correction to
O	5.82581000	-1.36705800	-0.16126400	Enthalpy= 0.249175
C	-2.35485300	0.53422300	-0.02045200	Thermal correction to
C	-1.75876500	-0.73427600	0.06375900	Gibbs Free Energy=
C	0.42347200	0.21146100	-0.03868900	0.184241
C	1.83732900	-0.17945300	-0.06608900	Sum of electronic and
C	-0.08925500	1.46929700	-0.12384600	zero-point Energies=
C	-1.51912500	1.69930800	-0.11798900	-1103.600517
C	-3.77236500	0.60654700	-0.00833900	Sum of electronic and
C	-2.50037900	-1.90396300	0.15834900	thermal Energies= -
C	-3.88707100	-1.78610600	0.16845800	1103.582362
C	2.84632300	0.71557900	0.32808900	Sum of electronic and
C	-4.53417200	-0.54350100	0.08505100	thermal Enthalpies=
C	2.18867600	-1.47166700	-0.48083200	-1103.581418
C	4.17303600	0.31863900	0.29377100	Sum of electronic and
C	3.52336900	-1.86207300	-0.51329200	thermal Free Energies=
C	4.51930700	-0.97322500	-0.12707800	-1103.646352
H	-2.01502000	-2.87104500	0.22323200	
H	2.60913100	1.71433900	0.67814400	
H	-5.61824900	-0.48125500	0.09309900	
H	1.42117700	-2.17278500	-0.78922700	
H	3.80610200	-2.85806200	-0.84033200	
H	0.09572500	3.33590000	-0.34128200	
H	-3.71164000	2.50828600	-0.15375400	
H	-5.55243300	-2.74708400	0.26675000	
H	4.89884700	2.00279000	0.91594000	
H	6.39297500	-0.63700500	0.14614700	

Name	QCT-70-anion			
Cartesian Coordinates	Energy			
O	-0.43098900	-0.89434000	0.06085200	Zero-point correction=
O	0.63551500	2.55920900	-0.25966500	0.217355
O	-4.44619500	1.75268100	-0.08370200	(Hartree/Particle)
O	-2.00720000	2.84017600	-0.21474500	Thermal correction to
O	-4.65442000	-2.96327600	0.27631500	Energy= 0.235164
O	5.17816900	1.16206400	0.66406600	Thermal correction to
O	5.81729200	-1.31999900	-0.15846400	Enthalpy= 0.236108
C	-2.39109900	0.49694900	-0.01927600	Thermal correction to
C	-1.79183600	-0.78112900	0.06705200	Gibbs Free Energy=
C	0.39019600	0.19281100	-0.04089800	0.171684
C	1.81023400	-0.18151100	-0.06821400	Sum of electronic and
C	-0.13648700	1.44071900	-0.12734000	zero-point Energies=
C	-1.57499300	1.65507600	-0.11936300	-1103.154294
C	-3.81800800	0.54412600	-0.00260100	Sum of electronic and
C	-2.51847000	-1.94721200	0.16313900	thermal Energies= -
C	-3.94639600	-1.89671300	0.18245000	1103.136485
C	2.80847600	0.19281100	0.32707900	Sum of electronic and
C	-4.56670700	-0.60099200	0.09393100	thermal Enthalpies=
C	2.17970200	-1.46861600	-0.48235800	-1103.135541
C	4.14070400	0.34483500	0.29396600	Sum of electronic and
C	3.51975300	-1.84276300	-0.51260500	thermal Free Energies=
C	4.50419900	-0.94204200	-0.12580600	-1103.199966

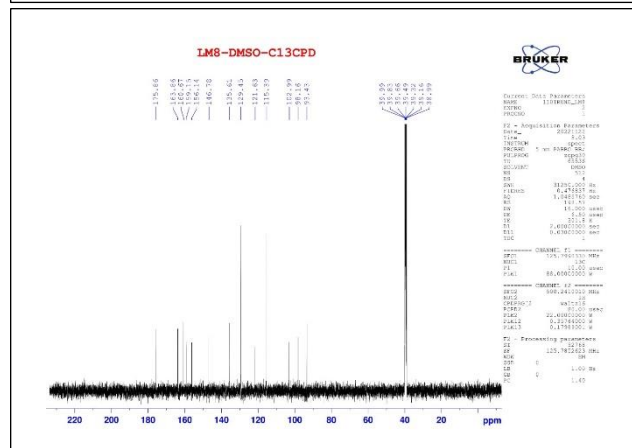
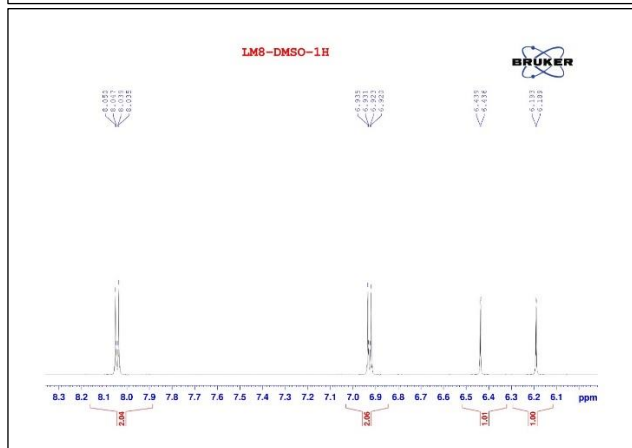
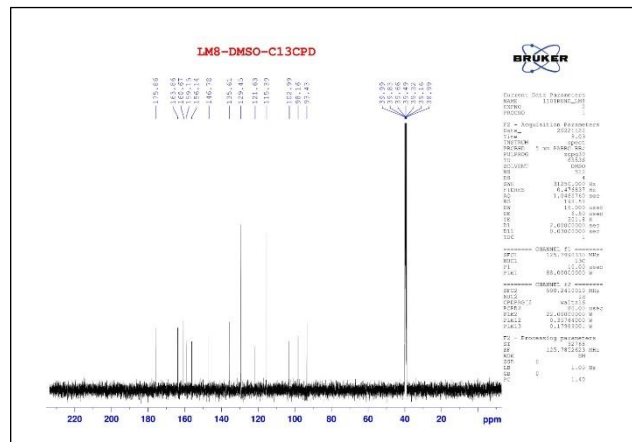
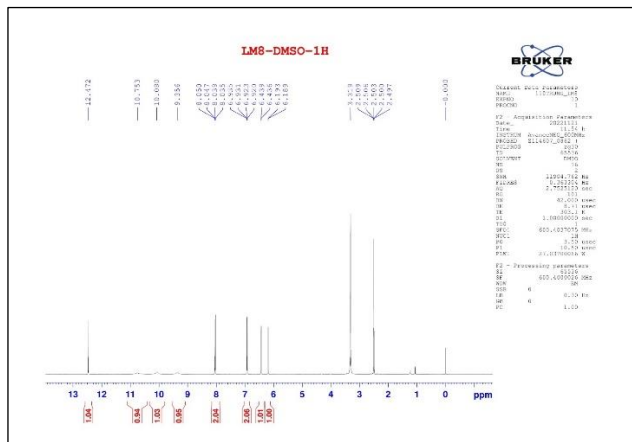
H	-2.00950300	-2.90363000	0.22807300	
H	2.55810800	1.72047800	0.67707400	
H	-5.65107700	-0.53631800	0.10497000	
H	1.42149300	-2.17973400	-0.79089000	
H	3.81491700	-2.83559100	-0.83859100	
H	0.00815500	3.30621600	-0.34771300	
H	-3.75243300	2.45053100	-0.15254900	
H	4.84323600	2.03864900	0.91786300	
H	6.37411500	-0.58249200	0.14958400	

Name	QCT-70-4'O-dianion			
Cartesian Coordinates	Energy			
O	-0.39815200	-0.89806200	0.05777900	Zero-point correction=
O	0.68534800	2.55383100	-0.26229600	0.204787
O	-4.39812700	1.76678400	-0.07883600	(Hartree/Particle)
O	-1.96085600	2.84283000	-0.21087200	Thermal correction to
O	-4.63242400	-2.95238700	0.26749300	Energy= 0.222177
O	5.20804500	1.17769700	0.65941100	Thermal correction to
O	5.85991000	-1.32035200	-0.14755200	Enthalpy= 0.223122
C	-2.35122700	0.49972900	-0.01619000	Thermal correction to
C	-1.75855300	-0.77901100	0.06331100	Gibbs Free Energy=
C	0.43519400	0.18253800	-0.04155400	0.159325
C	1.84291900	-0.19671200	-0.06685800	Sum of electronic and
C	-0.09663700	1.43544500	-0.12279800	zero-point Energies=
C	-1.52422600	1.65521100	-0.11373600	-1102.701612
C	-3.77570800	0.55375400	-0.00047100	Sum of electronic and
C	-2.49135400	-1.94366300	0.15436300	thermal Energies= -
C	-3.91787700	-1.88681500	0.17574000	1102.684221
C	2.86471900	0.70463500	0.31075000	Sum of electronic and
C	-4.53129400	-0.58876100	0.09205200	thermal Enthalpies=
C	2.21916700	-1.49193900	-0.45724800	-1102.683277
C	4.18825400	0.32021300	0.28433300	Sum of electronic and
C	3.55493600	-1.86959300	-0.48711500	thermal Free Energies=
C	4.60753600	-0.98921600	-0.12294500	-1102.747073
H	-1.98623900	-2.90247000	0.21574100	
H	2.61949800	1.70766900	0.64675600	
H	-5.61536400	-0.51793100	0.10302400	
H	1.45820000	-2.20814400	-0.75254300	
H	3.82824200	-2.87374900	-0.80319700	
H	0.05945500	3.30065700	-0.35515900	
H	-3.69673200	2.45842100	-0.14748600	
H	4.82788000	2.03794100	0.90204700	

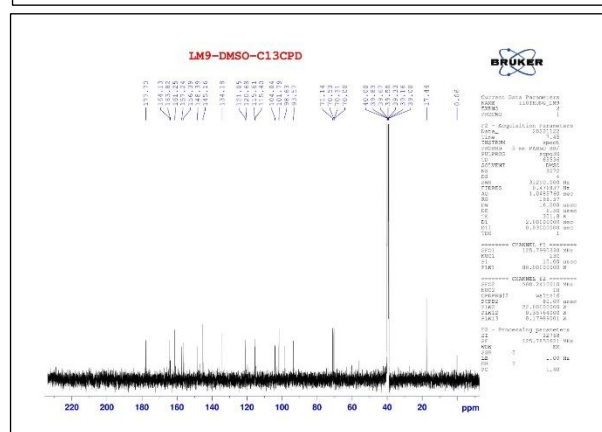
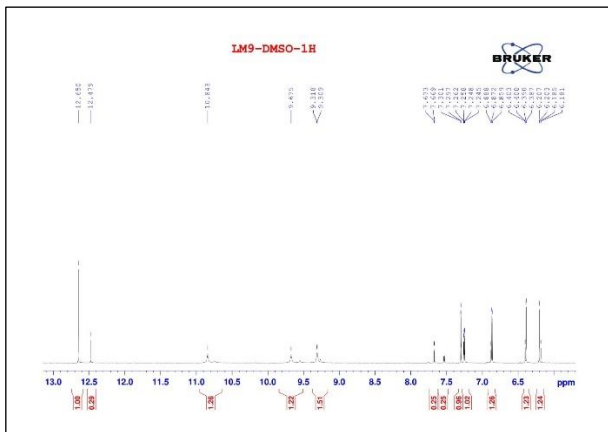
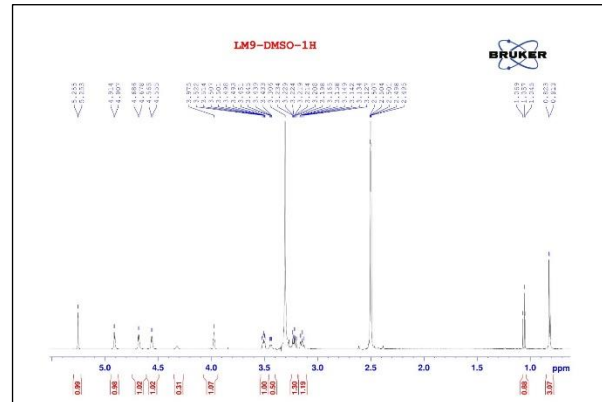
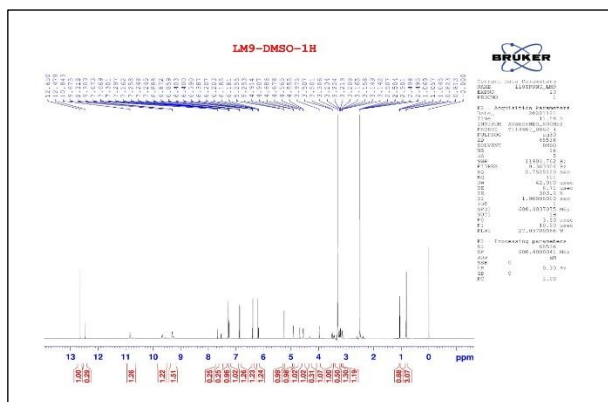
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Cartesian Coordinates	Energy			
O	1.98586400	-1.12059900	1.35375100	Zero-point correction=
O	0.51438100	-0.76286200	-0.42200100	0.400798
O	3.52289900	-3.50573700	-1.70149200	(Hartree/Particle)
O	5.02898400	-1.30399700	-0.64428900	Thermal correction to
O	1.98241100	-3.94018600	0.56081000	Energy= 0.429386
O	-2.29234200	1.48535800	-0.00014400	Thermal correction to
O	-1.61842700	-2.50712100	-0.34326900	Enthalpy= 0.430330
O	-4.21820900	-2.91438100	-0.09122700	Thermal correction to
O	-6.92860500	0.96921100	0.38158900	Gibbs Free Energy=
O	3.25735700	3.03918100	1.06926800	0.342813
O	2.75756000	5.15723100	-0.49737500	Sum of electronic and
C	2.91646300	-2.42914200	-1.00332500	zero-point Energies=
C	3.88001600	-1.82300500	0.00908400	-1638.795251
C	1.63564600	-2.87014500	-0.30705300	Sum of electronic and
C	3.20435700	-0.66504100	0.74047100	thermal Energies= -
C	1.04214600	-1.71611600	0.50525500	1638.766663
C	4.05782400	-0.10171500	1.85671200	Sum of electronic and
C	-0.75862600	-0.31352800	-0.17201400	thermal Enthalpies=
C	-1.02196800	1.02012600	-0.10230900	-1638.765719
C	-1.84059800	-1.28550800	-0.18743100	Sum of electronic and
C	-3.17222800	-0.74598100	-0.03063300	thermal Free Energies=
C	-3.35944500	0.64144000	0.05326400	-1638.853236
C	-0.04383600	2.11408900	-0.20091200	
C	-4.32771200	-1.57001300	0.00647700	

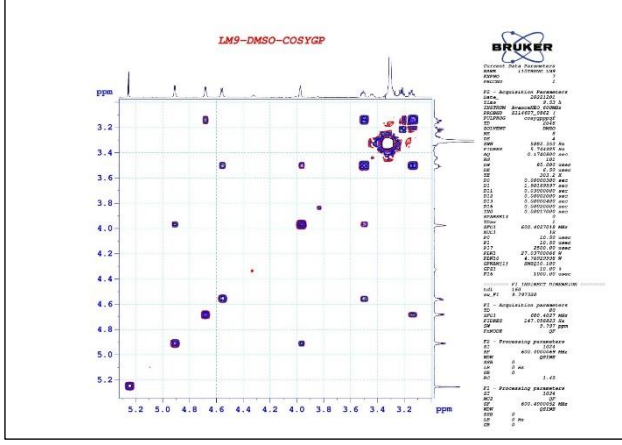
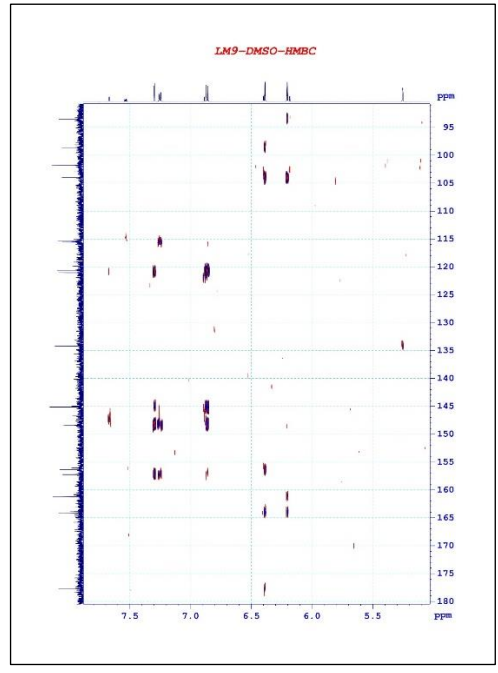
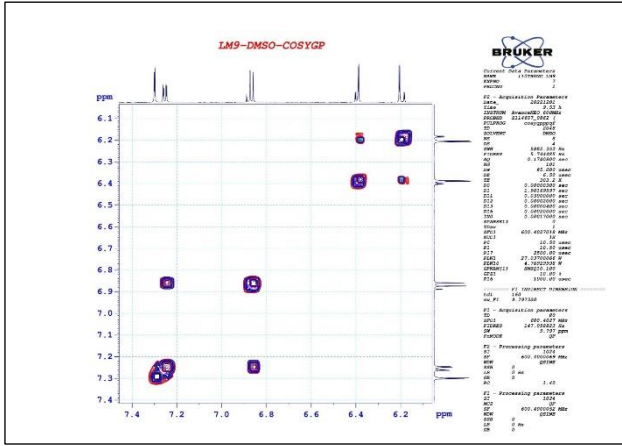
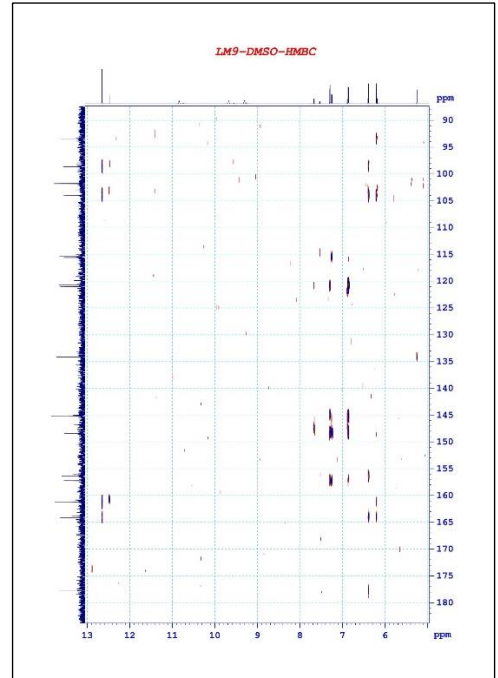
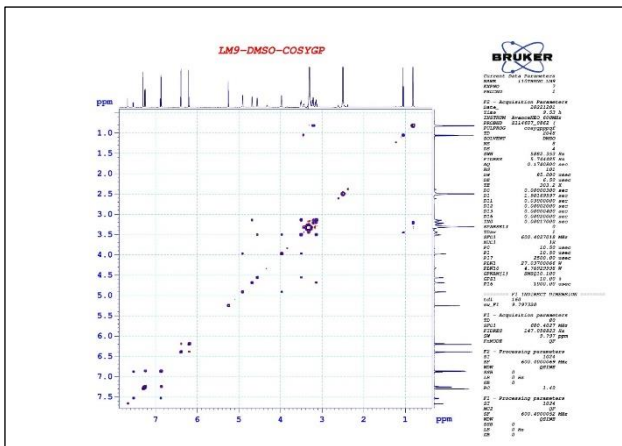
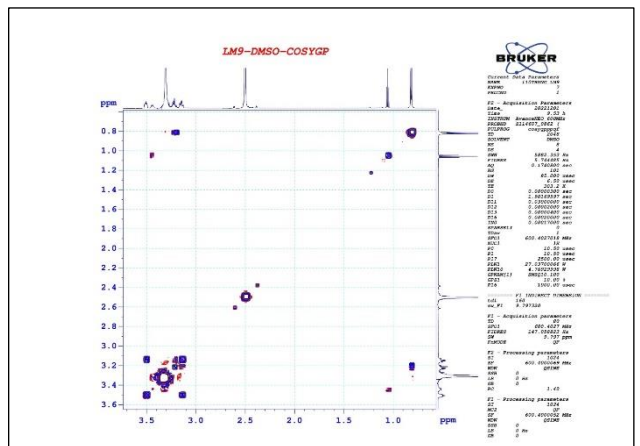
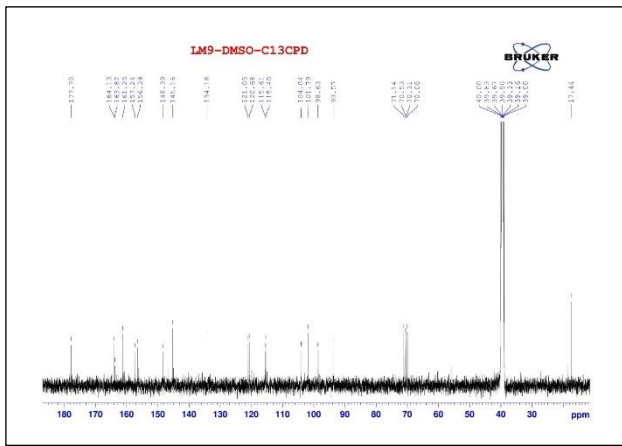
C	-4.60843600	1.22749200	0.19117200		H	4.29444500	-0.92525700	2.55266100	
C	1.16528200	2.05993900	0.50342500		H	4.92850000	0.32468200	1.45437300	
C	-0.33962300	3.22079600	-1.00386800		H	3.46777100	0.64475400	2.40859300	
C	-5.58670200	-1.01314200	0.14864000		H	3.53783900	-4.26552000	-1.09140700	
C	-5.71279600	0.38008800	0.24138300		H	5.33233600	-2.02108500	-1.22345800	
C	2.07826400	3.09502200	0.38038500		H	1.12604900	-4.44701800	0.77244100	
C	0.58166400	4.25762500	-1.12711300		H	-4.71324000	2.34513300	0.27229300	
C	1.78953900	4.19456000	-0.44202100		H	1.36142900	1.23173800	1.19290100	
H	2.67517600	-1.67060400	-1.75608600		H	-1.26541600	3.25511500	-1.56544000	
H	4.17749100	-2.58878000	0.74073900		H	-6.50716000	-1.61029500	0.17163200	
H	0.89966000	-3.19865700	-1.04711800		H	0.40331000	5.08994800	-1.78898400	
H	2.96688800	0.11563200	0.00308600		H	-3.31181700	-3.09395900	-0.20691000	
H	0.25130300	-2.08056800	1.16278100		H	3.76856200	3.82870500	0.90434400	
H	4.33736000	-0.89910300	2.55386300		H	2.51435800	5.84692000	-1.11240400	
H	4.96729800	0.34924400	1.45137900						
H	3.50470800	0.66725700	2.40337500						
H	3.59583100	-4.25248100	-1.08060500						
H	5.38171300	-2.00687000	-1.21596000						
H	1.17825200	-4.43911800	0.77809800						
H	-4.71829300	2.30390500	0.25682300						
H	1.38797600	1.22718100	1.16398800						
H	-1.27801300	3.26611700	-1.54722300						
H	-6.46361800	-1.65265600	0.18330900						
H	0.37323000	5.11834200	-1.75693200						
H	-3.26215900	-3.13203300	-0.21337700						
H	-7.63240800	0.29807700	0.41467800						
H	3.76631400	3.85186000	0.89963200						
H	2.48091100	5.88742900	-1.07694400						
Name				QCTR-7O-anion	Name				QCTR-7O-4'O-dianion
Cartesian Coordinates				Energy	Cartesian Coordinates				Energy
O	1.94201400	-1.13486400	1.35296000	Zero-point correction= 0.387744	O	2.02912000	-1.05021000	1.34298700	Zero-point correction= 0.375014
O	0.47182500	-0.76988100	-0.42355900	(Hartree/Particle)	O	0.50649000	-0.72783600	-0.39785700	(Hartree/Particle)
O	3.47178300	-3.51550100	-1.70909400	Thermal correction to	O	3.48972700	-3.51263200	-1.68424100	Thermal correction to
O	4.98315200	-1.31949500	-0.64804700	Energy= 0.416060	O	5.02984800	-1.29642900	-0.71084000	Energy= 0.402675
O	1.93179000	-3.95145600	0.55332200	Thermal correction to	O	1.99375300	-3.88686000	0.61379300	Thermal correction to
O	-2.30940700	1.50740000	0.02283700	Enthalpy= 0.417004	O	-2.33694200	1.48324100	0.02018000	Enthalpy= 0.403620
O	-1.66819500	-2.49920500	-0.33622700	Thermal correction to	O	-1.58573700	-2.50588800	-0.27761100	Thermal correction to
O	-4.27073500	-2.88594100	-0.08892100	Gibbs Free Energy= 0.329833	O	-4.17312500	-2.96020600	-0.04958900	Gibbs Free Energy= 0.317346
O	-6.97482600	0.97010200	0.36993500	Sum of electronic and	O	-6.99307800	0.82815100	0.29576100	Sum of electronic and
O	3.24846100	3.02606900	1.08718000	zero-point Energies= -1638.349447	O	3.27170200	3.13976000	0.90397300	zero-point Energies= -1637.901684
O	2.77888800	5.12813000	-0.51327800	Sum of electronic and	O	2.59790900	5.29007700	-0.50649200	Sum of electronic and
C	2.86783600	-2.43904300	-1.00806500	thermal Energies= 1638.321131	C	2.90295300	-2.41515400	-1.00088100	thermal Energies= -1637.901684
C	3.83341900	-1.83763100	0.00504500	Sum of electronic and	C	3.88937100	-1.78940900	-0.02304700	Sum of electronic and
C	1.58651400	-2.87854700	-0.31208900	thermal Energies= 1638.321131	C	1.63405800	-2.83253500	-0.26945500	thermal Energies= 1637.874022
C	3.16099300	-0.68050600	0.74096800	Sum of electronic and	C	3.23019100	-0.60952000	0.68713300	Sum of electronic and
C	0.99511500	-1.72406600	0.50112500	thermal Enthalpies= -1638.320187	C	1.05894100	-1.65913600	0.52942300	thermal Enthalpies= -1637.873078
C	4.01749700	-0.12425200	1.85858800	Sum of electronic and	C	4.10866600	-0.00617200	1.76242800	Sum of electronic and
C	-0.79736500	-0.30619500	-0.16318100	thermal Free Energies= -1638.407358	C	-0.77487400	-0.28853800	-0.13205400	thermal Free Energies= -1637.959352
C	-1.04409300	1.02697000	-0.08768900		C	-1.05084000	1.04740100	-0.07529500	
C	-1.89493900	-1.26956800	-0.17615300		C	-1.84088900	-1.27637300	-0.13700700	
C	-3.20578500	-0.72428000	-0.01760500		C	-3.17199000	-0.76884400	0.00093100	
C	-3.39533400	0.67219500	0.07332200		C	-3.39981600	0.62114200	0.06226300	
C	-0.05317000	2.11146000	-0.19326700		C	-0.10462000	2.15725100	-0.17474300	
C	-4.38422800	-1.53087200	0.01281800		C	-4.32652000	-1.60643000	0.02741700	
C	-4.63003200	1.26491000	0.20775700		C	-4.65371200	1.18243200	0.16532600	
C	1.15010000	2.05810800	0.52040700		C	1.16195400	2.10328100	0.44585400	
C	-0.33145500	3.20919800	-1.01441800		C	-0.45866300	3.30631200	-0.89561100	
C	-5.62996800	-0.96977100	0.14793000		C	-5.59057900	-1.07810300	0.13207000	
C	-5.80597300	0.45322200	0.25053000		C	-5.80702400	0.34044700	0.20457300	
C	2.07414100	3.08317200	0.38893400		C	2.03190800	3.16007300	0.30761400	
C	0.59973000	4.23661200	-1.14529700		C	0.42857200	4.37089000	-1.03014600	
C	1.80168000	4.17329300	-0.45038200		C	1.71109300	4.34149200	-0.43682000	
H	2.62793200	-1.67825300	-1.75898500		H	2.65081100	-1.67383700	-1.76714600	
H	4.13007500	-2.60629100	0.73402400		H	4.19540300	-2.53681400	0.72402500	
H	0.84990000	-3.20465800	-1.05258900		H	0.88336300	-3.17429600	-0.98788700	
H	2.92581100	0.10381300	0.00672400		H	2.97290300	0.14638400	-0.06912900	
H	0.20321800	-2.08778900	1.15765500		H	0.28743200	-2.01074500	1.21646100	
					H	4.40845800	-0.77793300	2.47983900	
					H	5.00615500	0.43387500	1.31998200	
					H	3.56589900	0.77950600	2.29574300	
					H	3.56342900	-4.24616300	-1.04780300	
					H	5.36442600	-2.01565700	-1.27300800	
					H	1.19061700	-4.37457700	0.85859800	
					H	-4.76699000	2.26103700	0.20956100	
					H	1.43843800	1.24870000	1.05597900	
					H	-1.43229100	3.35895300	-1.37529400	
					H	-6.44980500	-1.74274200	0.15293100	
					H	0.14519200	5.25040700	-1.60323100	
					H	-3.20548500	-3.13846700	-0.15372000	
					H	3.67562200	3.99997400	0.66374900	

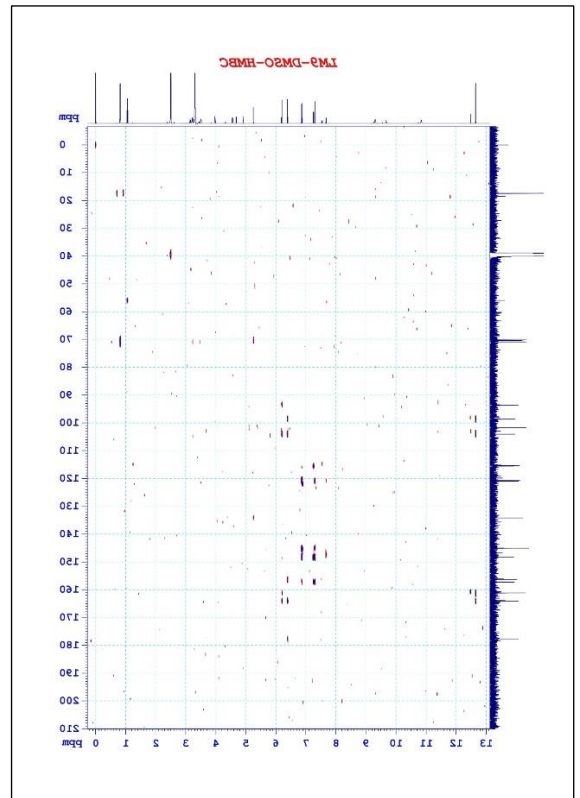
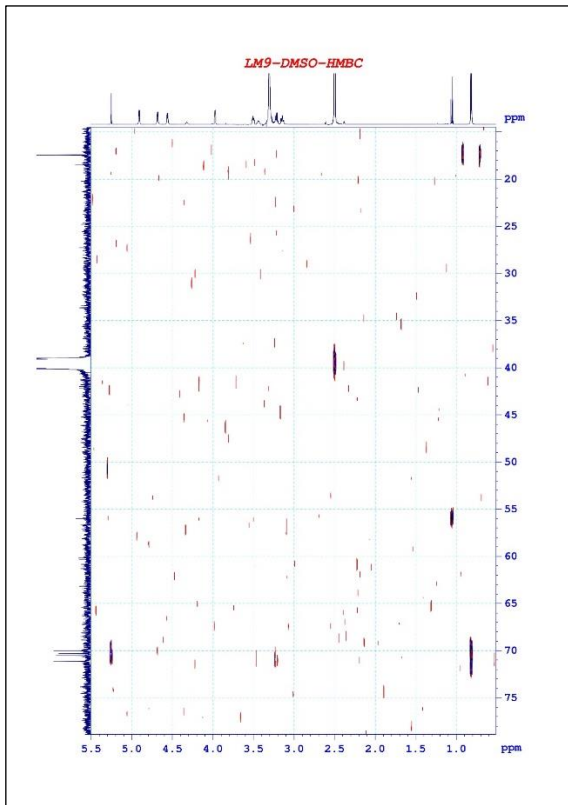
S5. NMR spectral of Kaempferol - LM8



S6. NMR spectral of Quercitrin - LM9







S7. NMR spectral of Quercetin - LM10

