

THE SULFONATION OF 3,5,7,3',4'-PENTAHYDROXYFLAVONE
AND NON-LINEAR-OPTICAL ACTIVITY
OF ITS SULFONIC DERIVATIVES*Dmytro Mishurov^{1, *}*<https://doi.org/10.23939/chcht13.01.033>

Abstract. Synthesis of sulfoquercetin and studies of its structure and nonlinear properties have been carried out. Using quantum-chemical simulations, ¹³C and HSQC NMR spectrometry, FTIR spectroscopy it was shown that a sulphonic group occurs in C₈ location of quercetin. Molecular first hyperpolarizability of the obtained 8-sulfoquercetin was studied. It was shown that 8-sulfoquercetin can be used for creation the new polymer NLO materials on its basis.

Keywords: quercetin, sulfonation, nonlinear activity, polarizability, property.

1. Introduction

At present, polymer and polymer composite materials are widely used in various nonlinear optical applications [1-3]. Besides regulating the NLO properties of polymer materials at a macroscopic level, an equally important task is to increase the molecular quadratic polarizability (β) values of the initial chromophores, because just the β values determine the macroscopic NLO properties of chromophore-containing polymers and polymer composite materials for these applications.

Several approaches to increase the parameter β of chromophores are well known. Firstly, this is a change in the structure of the electron-withdrawing and electron-donating groups [4]. Secondly, it is the introduction of suitable isolation groups (SIG) into the composition of the chromophores to reduce the dipole-dipole interaction between the chromophore molecules, as well as between the chromophore molecules and the polymer matrix with maintaining their asymmetric orientation. Thirdly, it is the increase of conjugation length [5].

Many electron-withdrawing and electron-donating substituted π -systems, including substituted benzenes, stilbenes, azobenzenes, and diphenylacetylenes (tolanes),

are known to display large NLO responses. However, the conjugated π -systems with common acceptor substituents such as NO₂, CN or COR have large molecular hyperpolarizabilities, they suffer from low optical transparency in the region of blue light due to charge-transfer (CT) self-absorption of chromophore ore chromophore moieties [6, 7].

In previous works [8-11] it was shown that donor-acceptor-substituted benzenes, styrenes, and tolanes with the sulfonic group as the acceptor substituent show a remarkable molecular nonlinearity combined with a charge-transfer absorption band at a relatively short wavelength.

Thus, the purpose of the paper is the chemical modification of 3,5,7,3',4'-pentahydroxyflavone by introducing the acceptor sulfonic group (SO₃H) into the chromophore molecule and investigation of nonlinear activity of its sulfonic derivatives.

In addition to the increase of nonlinear activity of modified chromophore, the multifunctional nature of sulfoquercetin may lead to easy chemical modification in order to obtain monomers for cross-linked polymers as NLO materials.

2. Experimental

2.1. Materials

Commercial 3,5,7,3',4'-pentahydroxyflavone (quercetin, $M_w = 302.24$, Sigma-Aldrich Chemicals) and sulfuric acid ($\rho = 1.84 \text{ g}\cdot\text{cm}^{-3}$) were used as investigation objects. A chemical structure of quercetin is shown in Fig. 1.

2.2. Synthesis of Quercetin-8-Sulfonic Acid (QSA-8)

8 cm³ of concentrated sulfuric acid ($\rho = 1.84 \text{ g}\cdot\text{cm}^{-3}$) was added to 2 g of quercetin in 100 cm³ round-bottom flask. The reaction mixture was vigorously stirred for 2 h at 291–293 K. Then, 20 cm³ of very cold water was added into the reaction mixture. The orange-red precipitate was

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filtered at a reduced pressure and recrystallized twice from the hot saturated water solution. Next, the orange-red sediment was dried in air at room temperature. The synthesis yield was 40 %. λ_{abs} (acetone) = 350 nm.

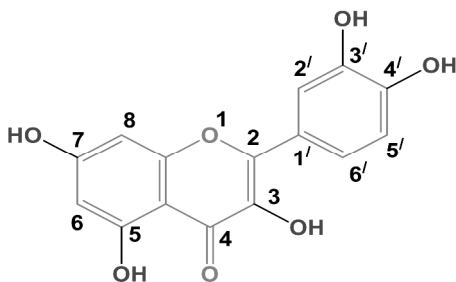


Fig. 1. Chemical structure of quercetin

Elemental Analysis: calc. (wt %): C-47,13; H-2,64; O-41,85; S-8,39. Found (wt %):. C-43,48; H-3,41; O-45,88; S-7,23.

^1H NMR (DMSO – d_6 , $J = 500$ MHz): 6.38 (d, 1H, $\text{C}^6\text{-H}$); 7.04 (d, 1H, $\text{C}^{5'}\text{-H}$); 7.53 (dd, 1H, $\text{C}^{6'}\text{-H}$); 7.67 (d, 1H, $\text{C}^{2'}\text{-H}$); 9,27 (d, 1H, $\text{C}^3\text{-OH}$); 9,31 (d, 1H, $\text{C}^{4'}\text{-OH}$); 9,56 (s, 1H, $\text{C}^{3'}\text{-OH}$); 10,76 (d, 1H, $\text{C}^7\text{-OH}$); 12,48 (s, 1H, $\text{C}^5\text{-OH}$).

2.3. Characterization

Unconstrained geometry optimizations of isolated molecules, calculations of Mulliken charges, free Gibbs energies and molecular quadratic polarizabilities of sulfonic derivatives in the ground singlet electronic state were carried out according to DFT theory [12] using the M062X functional [13] and cc-pVDZ basis sets [14, 15] implemented in the GAUSSIAN 09 program package [16]. The effect of the solvent (acetone) was included in the DFT calculations at the level of the polarized continuum model (PCM) [17, 18]. The calculations were carried out on the cluster of the Ukrainian-American Laboratory of Computational Chemistry (UALCC, Kharkiv, Ukraine).

UV-Visible spectra were recorded using an UV-Vis spectrophotometer Hitachi-U3210 in the range of 250–800 nm.

^1H and ^{13}C NMR spectra were measured on a Bruker AVANCE III NMR Spectrometer (500MHz) in DMSO- d_6 . Correlations between protons and carbons were assigned using the HSQC 2D NMR spectra.

FT-IR spectra were registered on a Spectrum One spectrophotometer (Perkin Elmer) in KBr in the range of 400–4000 cm^{-1} . The quantification of residual solvent is based on the strong absorption band located about 1720 cm^{-1} produced by the C=O group in the acetone molecule [19].

The elemental analysis was performed with an EA 1108 analyzer (Carlo Erba).

3. Results and Discussion

3.1. Quantum-Chemical Calculations of the Quercetin Sulfonation

Typically, oxygen-containing heterocyclic compounds hydrolyze in the presence of strong acids. But flavanols, to which 3,5,7,3',4'-pentahydroxyflavone belongs, is an exception. They are stable, both in concentrated sulfuric acid and its solutions with oleum. The reason for this stability is that in strongly acidic media, the carbonyl group of flavanols is protonated, resulting in the formation of a stable 2-phenyl-1-benzopyrylium (flavylium) cation. This fact must be taken into account when assessing the chemical activity of 3,5,7,3',4'-pentahydroxyflavone. Therefore, during the reaction of sulfonation, the SO_3H groups attack non-neutral quercetin molecule and the flavylium cation, which has another electron density distribution.

Geometry optimization of the initial 3,5,7,3',4'-pentahydroxyflavone molecule, its flavylium cation and possible sulfonation products, and then a further calculation of the charges on carbon atoms and the enthalpy of formation were carried out using the DFT method. Data of calculations are listed in Table 1.

As can be seen from Table 1, the most negative charges are characteristic for C_6 and C_8 atoms of chromone dicycle and C_3 atom in the side phenyl ring.

During the sulfonation under thermodynamic control, the most possible is formation of the 8-sulfoquercetin cation, although 3'-, 2'- and 6'-monosulfonic derivatives may be present in small amounts.

In addition, the formation of disulfonic derivatives of 3,5,7,3',4'-pentahydroxyflavone is possible. However, when forming such compounds, it should be taken into account that the second particle of HSO_3^+ is added to the cation containing the electron-withdrawing fragment of HSO_3 ; as a result the chemical reaction proceeds under more severe conditions and in the direction specified by the first sulfonic group. In this case, the most favorable is the sulfonation into different cycles of the 3,5,7,3',4'-pentahydroxyflavone molecule.

In the case of disulfonic derivatives (Table 2), the formation of the mixture of 8,2' and 8,5'-isomers is the most likely, as well as certain amount of 6,8-disulfonic derivatives. The presence of the latter is due to the meta-oriented effect of the sulfonic group that locates in C_8 position of a quercetin molecule.

Table 1

Theoretical values of the enthalpies of formation and geometric parameters of sulphonic derivatives of 3,5,7,3',4'-pentahydroxyflavone cations

Sulfonic group localization	* ΔH_f , kJ/mol	** φ , °	*** n , %
8	-730.19	21	89.82
6	-702.83	24	0.00
6'(1)	-709.69	54	0.02
6'(2)	-720.65	81	1.92
3'	-718.35	23	0.76
2'(1)	-716.18	48	0.32
2'(2)	-723.92	79	7.16

Notes: * ΔH_f is an enthalpy of molecule formation, kJ/mol; ** φ is the angle between the chromylum bicycle and the side phenyl ring; *** n is the molar concentration of the components in the mixture.

Table 2

Theoretical values of the enthalpies of formation and geometric parameters of sulfoflavylium of 3,5,7,3',4'-pentahydroxyflavone cations

Sulfonic group localization	ΔH_f , kJ/mol	φ , °	n , %
8,6	-1178.63	13	0.28
6,2'	-1174.45	80	0.05
6,5'	-1171.06	23	0.01
6,6'	-1158.17	77	0.00
8,2'	-1191.52	43	51.02
8,5'	-1191.39	19	48.50
8,6'	-1176.58	58	0.12
6',2'	-1170.77	90	0.01
6',5'	-1165.62	80	0.00
5',2'	-1150.06	68	0.00

Table 3

Chemical shifts of carbon atoms in the ^{13}C NMR spectra of the initial quercetin and quercetin-8-sulphonic acid (ppm)

Substances	6	8	2'	5'	6'
Quercetin	98.50	93.70	115.40	116.10	120.70
Quercetin-8-sulphonic acid	98.62	93.94	115.51	116.05	120.50
$\Delta\delta$	-0.12	-0.24	-0.11	0.05	0.20

3.2. Determination of the Localization of the Sulfonic Group Using the NMR Method

To determine the location of sulfonic group attachment in the 3,5,7,3',4'-pentahydroxyflavone molecule two methods (^{13}C NMR and HSQC NMR) were used.

A comparison of the experimental ^{13}C NMR spectra of the initial quercetin and sulfoquercetin (Table 3) shows that the resulting substance has only one sulfonic group in the C₈ position. This is evidenced by the fact that the greatest chemical shift ($\Delta\delta$) of the carbon atom occurs into the area of lower fields in the C₈ position, when the

initial quercetin sulfonation is observed. This phenomenon is explained by the fact that descreening of this carbon atom takes place due to the incorporation of a strong acceptor.

It should also be noted that for aromatic systems (to which quercetin belongs) there is one mechanism of electrophilic substitution – S_EAr (electrophilic aromatic substitution). S_EAr reaction is the most common and most important one among aromatic substitution reactions.

Substituents in the benzene ring can both promote the substitution reaction (activation using substituents) and inhibit the reaction rate (deactivation using substituents). Some groups orient substitution in *ortho*- and *para*-position, others – in *meta*-position. The

quercetin has OH substituents in *ortho*- and *para*-position, activating the S_EAr reaction.

In two-dimensional HSQC spectrum of sulfoquercetin, there are four “spots” (Fig. 1) corresponding to the signals of the hydrogen atoms at the carbon atoms at the C_6 , C_6' , C_5' and C_2' positions. The “spot” corresponding to the hydrogen at the carbon C_8 atom is absent, which confirms the earlier conclusions based on the ^{13}C NMR analysis. Thus, the resulting substance is 3,5,7,3',4'-pentahydroxyflavone-8-sulfonic acid.

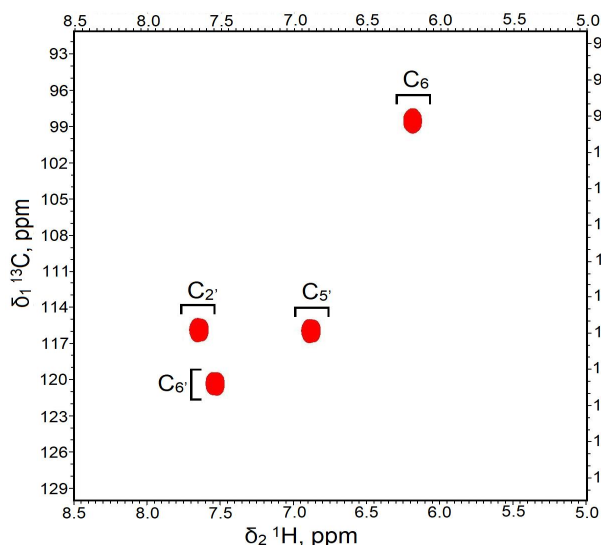


Fig. 2. HSQC ЯМР spectrum of 3,5,7,3',4'-pentahydroxyflavone-8-sulfonic acid

3.3. FTIR Analysis

The structures of pure quercetin and quercetin-8-sulfonic acid were confirmed by FTIR spectral analyses. The FTIR spectra (Fig. 2) of all specimens have a broad absorption band at 3178–3500 cm^{-1} region assigned to the stretching vibration of phenyl OH groups and OH groups in a water. The C–H asymmetrical and symmetrical stretching vibrations of the methyne (CH) and methylene (CH_2) groups are observed around 2920 and 2850 cm^{-1} region, respectively. The absorption bands which characterize deformation vibrations of CH groups occur around 1380–1300 cm^{-1} and of CH_2 groups between 1453–1429 cm^{-1} . The peak observed between 1641–1750 cm^{-1} is due to the presence of the carbonyl group stretching vibrations. The C=C–C stretching vibrations are observed around 1580–1618 cm^{-1} and 1510–1450 cm^{-1} regions. The absorption band at 691 cm^{-1} may be attributed to deformation vibrations of an aromatic ring.

In FTIR spectrum of the quercetin-8-sulfonic acid the absorption band is present at 1031 cm^{-1} , which characterizes the symmetric stretching vibrations of the sulfonic group [20].

Thus, it should be noted that the basic substance, which is obtained under the synthesis condition, is quercetin-8-sulphuric acid. The quantum-chemical calculations are in very well correlation with the experimental data.

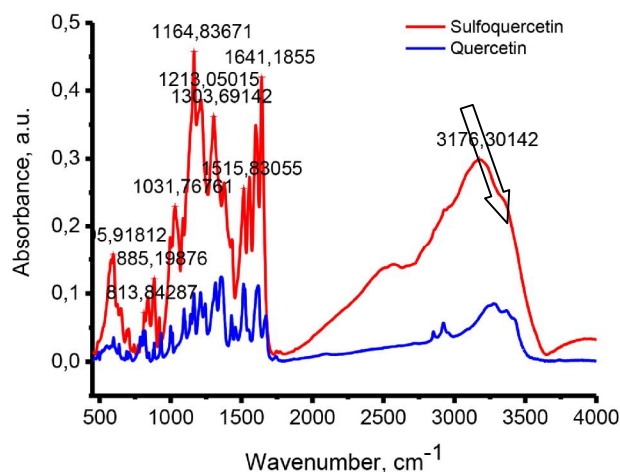


Fig. 3. FTIR spectra of initial quercetin (1) and quercetin-8-sulphuric acid (2)

3.4. Nonlinear Optical Properties of Quercetin-8-Sulphuric Acid

The molecular first hyperpolarizabilities (β) and ground-state dipole moments (μ_g) of initial quercetin, and quercetin-8-sulphuric acid were compared. The values of β and μ_g for pure quercetin were equal to $54.1 \cdot 10^{-40} m^4/V$ and $1.2199 \cdot 10^{-29} C \cdot m$, respectively. At the same time, similar values for quercetin-8-sulphuric acid were $62.1 \cdot 10^{-40} m^4/V$ and $5.7544 \cdot 10^{-29} C \cdot m$, respectively. Thus, it can be seen that the values of β and μ_g for quercetin-8-sulphuric acid are higher than those for the initial quercetin. In our opinion, this can be explained by the fact that in the quercetin-8-sulphuric acid the charge value on the chromylum bicycle increases with the decrease of substituents donor strength in the side phenyl ring leading to the increase in the ground-state dipole moment. With the increase of μ_g values in quercetin-8-sulphuric acid molecule the redistribution of electron density occurs and they become more non-symmetrical resulting in the increase of non-linear optical activity.

4. Conclusions

Thus, the structure of sulfoquercetin was established. Based on the results of quantum-chemical calculations, ^{13}C NMR analysis, HSQC method and FTIR analysis, it was concluded that the sulfonation of the

initial quercetin is the most probable by the electrophilic substitution mechanism. In this case, a monosulfonic derivative having only one sulpho group at the C₈ position is formed. A physico-chemical analysis of the obtained sulfonic derivative of 3,5,7,3',4'-pentahydroxyflavone was carried out. It was established that the non-linear optical properties of sulfoquercetin molecules are higher than of the initial quercetin, which is due to the redistribution of the electron density in the sulfonation process. The high non-linear optical activity of 8-sulfoquercetin makes this substance promising for the creation of NLO polymers and polymer composite materials.

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СУЛЬФУВАННЯ 3,5,7,3',4'-ПЕНТАГІДРОКСИФЛАВОНУ ТА НЕЛІНІЙНО ОПТИЧНІ ВЛАСТИВОСТІ ЙОГО СУЛЬФОПОХІДНИХ

Анотація. Проведено синтез сульфокверцетину та вивчення його структури й нелінійно оптичних властивостей. Із використанням квантово-хімічних розрахунків, ¹³C і HSQC ЯМР спектроскопії, ІЧ спектроскопії було показано, що сульфонова група в знаходиться у положенні C₈ кверцетину. Визначено молекулярну гіперполяризованість отриманого сульфокверцетину. Показано що сульфокверцетин можливо використовувати для створення на його основі нових полімерних НЛО матеріалів.

Ключові слова: кверцетин, сульфування, нелінійно-оптична активність, поляризованість, властивості.