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Syntheses, crystal structures and antioxidant study of Zn(II) complexes with morin-5′-sulfonic acid (MSA)

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ABSTRACT

The study of modified synthetic procedure of water soluble morin-5′-sulfonic acid sodium salt (NaMSA) involving less aggressive chemicals and carried out at mild conditions was described. The NaMSA salt is a convenient source of anionic morin-5'-sulfonic ligand (MSA) in ion exchange reactions. The coordination ability of MSA ligand towards the zinc cations was investigated in aqueous solution and in solid state. Novel zinc complexes of morin-5'-sulfonate were obtained by a reaction of $Zn(NO_3)_2$ with morin-5'-sulfonate in water. Resulting compounds were characterized by single-crystal X-ray diffraction analysis, as well as spectral and thermal methods. The coordination interaction, hydrogen bond and π–π stacking lead to the formation of a 1D chain or 3D coordination polymers. The antioxidant activity of the Zn(II)–MSA complexes was evaluated by means of 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging method. In this work, we have shown that the studied compounds are more effective free radical scavengers than the natural flavonoids like plain morin.

1. Introduction

Morin (2′,3,4′,5,7-pentahydroxyflavone) is a natural plant dye belonging to the flavonol class of flavonoids, a group of low cytotoxicity polyphenols existing widely in fruits and vegetables. These natural compounds possess potential antibacterial, anticancer, antioxidant, anti-inflammatory, and antiallergic properties since they are able to stimulate or inhibit a wide variety of enzyme systems. Thus, they are extensively used as pharmacological agents [1,2]. The bioactivity of morin and other hydroxyflavonoids is related to their metal-ion chelating ability and a free radical scavenging activity. Due to suitable arrangement of the hydroxyl groups in the molecule, morin easily forms complexes by chelating p-, d-, and f-electron metals ions [3–9]. It is worth notice, that metal complexes of flavonoids may exhibit higher antioxidant abilities than flavonoids themselves [10–13]. However, to date no X-ray crystal structures of morin complexes have been reported [14]. There have only been known molecular structures of two morin hydrates [15]. This is probably due to the limited solubility of flavonoids in purely aqueous solution and near the physiological values of pH. As a result, most of the studies with hydroxyflavonoids acting as a ligand for the metal complexes have been performed in mixed or non-aqueous solvent systems. The complex species formed in an aqueous solution remain unclear and still need to be researched [16]. Hence, sulfonic derivatives of flavonoids which exhibit improved solubility in water appear to be a promising choice for studying [17]. Moreover, these derivatives are claimed to retain the properties of the parent compound [18]. Research on magnesium(II) and iron(II) complexes of sulfonic derivatives of quercetin (QSA) and morin (MSA) has had great importance recently because of the anticarcinogenic effect shown by those complexes [19]. Moreover, substitution of the sulfo group at position 5′ on the lateral phenyl ring enhances anti-staphylococcal activity of flavonoids [20]. Nevertheless, the influence of sulfonato substituent on the crystal structure and bioactivity of flavonoid derivatives is still discussed [16,21]. Until now, crystal structures of a few sulfonic derivatives and their salts have only been reported: ammonium quercetin-5′-sulfonate [22], sodium quercetin-8-sulfonate trihydrate [23], potassium mikanin-3-O-sulfate [24], salts of 6-sulfonate derivative of chrysin with calcium [25], cadmium [26] and barium [27] ions.

Herein, we present a modified synthesis of the water soluble sodium salt of morin-5′-sulfonic acid (NaMSA hydrate) and show a very interesting behavior of the morin-5′-sulfonic ligand (MSA) at water environment in the presence of Zn(II) ions. The comprehensive data obtained from single-crystal X-ray experiments, spectroscopic measurements and thermal analysis allow us to characterize compounds extensively. These data have an important role in understanding chemistry of the sulfonated flavonoid ligand type better in presence of metal ions widely involved within biological systems.

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2. Experimental

2.1. Materials

All reagents were of analytical grade and were used as received without further purification. Both morin hydrate (2-(2,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-one), as well as DPPH (2,2′-diphenyl-1-benzopyran-4-one) were purchased from Sigma-Aldrich; H_2SO_4 ($d = 1.84$ g ml^{-1}), while NaOH, $ZnSO_4 \times 7H_2O$, $Na_2H_2edta \cdot 2H_2O$, chloric(VII) acid and HPLC grade methanol were purchased from POCh Poland. All the aqueous solutions were freshly prepared using double distilled water.

2.2. Instrumentation

Elemental analyses for C, H and S were performed with an Elemental Analyzer EA 1108 apparatus (Carbo Erba, Italy). The content of Na was determined by an AAS Perkin Elmer 3100 spectrophotometer (Perkin Elmer, USA). The thermogravimetric method was applied to find the content of crystallization water in the compounds. The total amounts of zinc were determined by titration with Na_2H_2edta solution. The UV–vis spectra were obtained by Jasco UV–vis-NIR V670 double beam spectrophotometer using 1.00 cm quartz cells in water and methanol solvent. The ^{1}H NMR spectra in DMSO-d_6 were recorded on a Bruker Avance II 500 MHz NMR spectrometer. The IR spectra were recorded by using KBr pellets in the spectral range of 4000–400 cm^{-1} on a FT-IR ALPHA-T (Bruker, Germany) instrument. Raman spectra of crystalline materials were recorded with a cm^{-1} in the range 100–1800 cm^{-1}. The laser source wavelength used was 780 nm. The spectral resolution was about 2 cm^{-1} for all measurements. Thermogravimetric analysis (TGA) was performed with a TGA/DSC 1 apparatus (Mettler Toledo) in the temperature range of 25–800 °C in air, with a heating rate of 10 °C min^{-1}. The differential scanning calorimetry (DSC) curve was obtained by DSC Q200 (TA Instruments), between 25 and 800 °C, the heating rate of 10 °C min^{-1}. The single crystal X-ray diffraction data were collected at 100.0(2) K on a Gemini A Ultra (Agilent Technologies) diffractometer.

2.3. Synthesis and characterization of the compounds

2.3.1. Preparation of morin-5′-sulfonic acid sodium salt (NaMSA) (**1**)

In a 100 ml round-bottomed flask, 18 ml of concentrated H_2SO_4 ($d = 1.84$ g ml^{-1}) was added to 15 g of morin hydrate. The reaction mixture was stirred for 3 h at 70 °C (±2 °C). Then, 80 ml of double distilled water was added into the reaction mixture. The post-sulfonic mixture was neutralized with a 20% aqueous solution of NaOH up to pH = 3. The precipitated brown solid was filtered off and recrystallized several times from a saturated hot aqueous solution yielding yellow microcrystalline material.

*2.3.1.1. Characterization of **1***. Yellow solid, Yield: 60%. ^{1}H NMR; (DMSO-d_6, 500 MHz): δ 6.19 (s, 6H, Ar), 6.35 (s, 8H, Ar), 6.31 (s, 3′H, Ar), 7.51 (s, 6′H, Ar), 10.75 (d, 3OH-Ar), 12.56 (s, 5OH-Ar), 10.76 (d, 7OH-Ar), 8.96 (s, 2′OH-Ar), 10.03 (s, 4′OH-Ar), 3.40 (s, H_2O). FT-IR; (KBr, cm^{-1}): 3700–2100 (3441, 3097, 2710, 2591) br, 1660 s, 1606 s, 1573 s, 1550 s, 1512 s, 1431 s, 1400 s, 1356 s 1299 s, 1250 s, 1215–1145 (1197, 1170) br, 1176 s, 1081 s, 1020 s, 1006 s, 974 m, 918 w, 884 w, 836 m, 728 m, 710 m, 679 m, 659 m, 587 m, 520 w, 469 w. Raman (cm^{-1}): 1656w, 1614 m, 1604s, 1574s, 1545 m, 1514s, 1396 m, 1392 m, 1356vs, 1322w, 1261s, 1207w, 1173w, 1080w, 1021w, 934w, 932w, 883w, 760 m, 733w, 655w, 586 m, 584 m, 521 m, 479 m, 444w, 424w, 344w, 308w, 251w, 198w, 147 m, 117 m. UV–vis; (water, λ_{max}, nm ($\varepsilon_{max}/10^4$, M^{-1} cm^{-1})): 374 (1.37), 260 (2.01); (methanol, λ_{max}, nm ($\varepsilon_{max}/10^4$, M^{-1} cm^{-1})): 358 (1.38), 254 (2.18). Anal. Data Calc. for [$C_{15}H_9O_{10}SNa$ 3.5H_2O] (467.33 g mol^{-1}): C, 38.55; H, 3.45; S, 6.86; H_2O, 13.49; Na, 4.92%. Found: C, 38.24; H, 3.16; S, 7.15; H_2O, 13.91; Na, 4.73%.

2.3.2. Preparation of the Zn(II) complex with morin-5′-sulfonic acid: ZnMSA (**2**)

The solutions of NaMSA ($c_L = 0.01$ M) and of $ZnSO_4$ ($c_M = 0.05$ M) were prepared by dissolving the appropriate weighed amounts of compounds in double distilled water. Additionally, the solution of $ZnSO_4$ was acidified (pH = 1.7) using a 1 M H_2SO_4. The synthesis was performed at the mole ratio MSA ligand to zinc cation M:L = 3:1. Stock solution (50 ml) of NaMSA (0.5 mmol) was added into 30 ml of solution of $ZnSO_4$ (1.5 mmol). Then, the reaction mixture was neutralized to pH = 4 by means of 0.1 M NaOH solution and heated for 2 h at 70 °C (±2 °C). After 24 h, yellow precipitate was filtered off, rinsed several times with distilled water/methanol solution and dried in the air at room temperature.

*2.3.2.1. Characterization of **2***. Yellow crystals, Yield: 58%. ^{1}H NMR; (DMSO-d_6, 500 MHz): δ 6.22 (s, 6H, Ar), 6.44 (s, 8H, Ar), 6.24 (s, 3′H, Ar), 7.83 (s, 6′H, Ar), 12.97 (s, 5OH-Ar), 11.54 (d, 7OH-Ar), 10.77 (s, 2′OH-Ar), 10.96 (s, 4′OH-Ar), 3.35 (s, H_2O). FT-IR; (KBr, cm^{-1}): 3700–2000 (3362, 2746, 2604) br, 1651 s, 1617 s, 1598 s, 1538 s, 1508 s, 1474 s, 1445 s, 1365 s 1331 s, 1309 s, 1246 s, 1224–1131 (1206, 1170) br, 1170 s, 1124 s, 1108 s, 1087 s, 1020 s, 1006 s, 980 s, 899 m, 840 m, 791 m, 747 m, 709 m, 685 s, 653 s, 635 s, 583 s, 561 m, 549 m, 518 m. Raman (cm^{-1}): 1652 m, 1627w, 1601w, 1546vs, 1534s, 1505s, 1492 m, 1489 m, 1486 m, 1446w, 1444w, 1409vs, 1377w, 1328w, 1265s, 1200w, 1184 m, 1108w, 1092w, 1023w, 1007w, 979w, 901 m, 748 m, 727w, 657w, 592w, 585w, 581 m, 521 m, 475w, 440w, 404w, 307w, 225w, 152w. UV–vis; (methanol, λ_{max}, nm ($\varepsilon_{max}/10^4$, M^{-1} · cm^{-1})): 412 (2.66), 266 (2.67). Anal. Data Calc. for [$ZnC_{15}H_8O_{10}S$ 3.5H_2O] (508.70 g mol^{-1}): C, 35.41; H, 2.97; S, 6.30; Zn, 12.85; Na, 0.00; H_2O, 12.39%. Found: C, 34.52; H, 2.78; S, 6.24; Zn, 12.46; Na, 0.00; H_2O, 12.68%.

2.3.3. Preparation of complex $Na_2Zn(MSA)_2$ (**3**)

Complex **3** was obtained following the same general procedure as for **2** with mole ratio M:L = 1:3 using 90 ml of NaMSA (9 mmol) and 6 ml of $ZnSO_4$ (3 mmol) solutions. Precipitated crystalline material was characterized by elemental analysis, as well as UV–vis, and IR spectroscopy.

*2.3.3.1. Characterization of **3***. Brick red crystals, Yield: 27%. ^{1}H NMR; (DMSO-d_6, 500 MHz): δ 6.1844 (d, 6H, Ar), 6.4077 (s, 8H, Ar), 6.2390 (d, 3′H, Ar), 7.8196 (s, 6′H, Ar), 12.9212 (s, 5OH-Ar), 11.5658 (s, 7OH-Ar), 10.7298 (s, 2′OH-Ar), 10.8691 (s, 4′OH-Ar), 3.3448 (s, H_2O). FT-IR; (KBr, cm^{-1}): 3700–2000 (3417, 2734, 2626) br, 1654 s, 1605 s, 1541 s, 1507 s, 1469 s, 1436 s, 1363 s 1318 s, 1299 s, 1250 s, 1203 s, 1178 s, 1143 s, 1102 s, 1087 s, 1029 s, 1011 s, 981 s, 911 m, 848 m, 834 s, 792 m, 739 m, 726 m, 713 m, 684 s, 654 s, 637 s, 580 s, 556 s, 555 s, 524 m, 465 m. Raman (cm^{-1}): 1653 m, 1604w, 1551 m, 1535s, 1533s, 1510s, 1508s, 1486w, 1434 m, 1404w, 1361s, 1282w, 1247vs, 1198w, 1178w, 1125w, 1025w, 980vw, 901w, 756 m, 748 m, 730w, 655w, 616w, 585 s, 524 m, 471 m, 435w, 383w, 293w, 248w, 195w, 168w, 133w. UV–vis; (methanol, λ_{max}, nm ($\varepsilon_{max}/10^4$, M^{-1} · cm^{-1})): 404 (4.63), 266 (5.09). Anal. Data Calc. for [$Na_2Zn(C_{15}H_8O_{10}S)_2$ 8H_2O] (1016.03 g mol^{-1}): C, 35.46; H, 3.17; S, 6.31; Zn, 6.44; Na, 4.53; H_2O, 14.18%. Found: C, 35.60; H, 3.24; S, 5.53; Zn, 6.47; Na, 4.76; H_2O, 10.62.%.

The solubility of the compounds in water at 20 °C is: 2.7×10^{-2} M (1.108 g/100 g soln.) [17] for **1** and 3.9×10^{-4} M (2.0×10^{-2} g/100 g soln.) and 1.0×10^{-3} M (10.4×10^{-2} g/100 g soln.) for **2** and **3** respectively.