



Crystal structure, spectroscopic properties and antimicrobial activity of 4H-1-Benzopyran-4-one, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl from *Miconia ioneura* Griseb. Melastomataceae

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ABSTRACT

From the bioactive ethyl acetate extract of leaves of *Miconia ioneura* Griseb (Melastomataceae) we isolated a flavone as a microcrystalline solid. This substance was identified as 4H-1-Benzopyran-4-one,5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl (sideroxylin) by melting point and IR of the solid and by NMR and UV spectroscopic techniques in solution. Furthermore, we succeeded in growing single crystals adequate for structural studies. The molecular structure of sideroxylin, C₁₈H₁₆O₅, has been determined by X-ray diffraction methods at 150K. The substance crystallizes as a monohydrate in the monoclinic P2₁/c space group with a=7.322(1), b=17.014(2), c=12.210(1) Å, β=93.73(1)°, and Z=4 molecules per unit cell. The fused phenyl and hetero-cycle rings are coplanar to each other and the phenyl group which is σ-bonded to the latter ring belongs closely to that plane. Observed intra-molecular distances and angles complain with the bonding structure expected from the Organic Chemistry rules. The molecule presents a strong intra-molecular O-H...O bond.

As a result of antimicrobial tests with ethyl acetate extracts and sideroxylin we found antifungal activity of both substances against several *Candida* strains.

Keywords: *Miconia ioneura*, Melastomataceae, Sideroxylin, Structure elucidation, Antimicrobial activity.

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Introduction

As part of our research dealing with bioactive constituents from northwestern Argentinean flora, we have undertaken studies on *Miconia ioneura*. *Miconia* is the largest genus of *Melastomataceae* family with about 1000 species widely distributed in the World [1]. Species of this family has been used in folk medicine, especially in Asia and America Latina, as haemostatic, astringents, dysenteric and in the treatment of skin diseases, respiratory and urinary affections [2].

M. ioneura grows in Yungas zone, in Tucumán, Argentina. Many species of the genus *Miconia* have showed different biological activities such as analgesic effect [3,4] and trypanocidal activity [5,6], while *M. ciliata* is traditionally used for cold treatment [7]. *M. coronata* has showed ichthyotoxicity effects [2]. Phytochemical investigations of *Miconia* species have resulted in the isolation of triterpenes, flavanones, quinone, and quinol compounds [1]. Extracts of *Miconia* species (*M. albicans*, *M. rubiginosa* and *M. stenostachya*) exhibited antimicrobial effect against some tested microorganisms such as *Candida albicans* [8]. Phenolic compounds from *Miconia myriantha* have showed inhibitory effects against *Candida albicans* secreted aspartic proteases (SAP), one the major virulence factor in *Candida* infections. Inhibition of SAP has been proposed as a new approach in the treatment of candidosis [9].

We show here that the ethyl acetate extract of *Miconia ioneura* leaves and one of its isolated compounds present antifungal activity. From active ethyl acetate extract of *M. ioneura* we isolated 4H-1-Benzopyran-4-one, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl (**1**) (sideroxylin), solved its molecular structure by single crystal X-ray diffraction methods and studied it in solution by NMR and UV spectroscopic techniques. We also briefly discuss here the IR spectrum of **1** in the solid state. The compound has also been found in the genus *Eucalyptus* and only in the families *Didieriaceae*, *Ericaceae*, *Guttiferae*, *Myrtaceae* and *Pinaceae* [10]. To the best of our knowledge, this is the first time that sideroxylin has been isolated from the *Melastomataceae* family.

Experimental

General Experimental Procedures

Melting point was measured on a Mikroskop heiztisch 350. Leitz. Germany. UV spectra were recorded on a Hewlett-Packard 8253 spectrometer. FTIR absorption data were collected

on a PerkinElmer 1600 spectrophotometer with a resolution of 2 cm^{-1} by accumulating 16 scans in the spectral region between 4000 and 400 cm^{-1} . Powdered samples of the extracts were mixed with KBr and prepared as pellets for the IR measurements. The NMR spectra were recorded on a Varian Gemini 2000 spectrometer at 200 MHz for ^1H .

Plant Material

Miconi ioneura Griseb. (Melastomataceae) used in this study was collected in El Indio, Tafi del Valle (at approximately 800 meters above sea level), Tucumán. A voucher specimen has been deposited at the Herbarium of Miguel Lillo Foundation (voucher N° 594108), Tucumán, Argentina.

Extraction and Isolation

Dried leaves of *M. ioneura* (386.96 g) were extracted with ethyl acetate at room temperature during 48 hs and then submitted to reflux during 4 hours. The solvent was evaporated at room temperature and the extract (5.5480 g) was suspended in hexane (50 ml) and extracted with methanol/ H_2O 80:20 (200 ml). The methanol/ H_2O fraction was suspended in methanol/ H_2O (60:40) and then extracted with chloroform. This solution was allowed to evaporate at room temperature to precipitate the **1** compound (45 mg) as a microcrystalline solid. Then, the crystals were washed three times with benzene.

4H-1-Benzopyran-4-one, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl (**1**) light yellow needles mp 271-273 °C. UV (MeOH) λ_{max} (log ϵ): 328 (4.20), 279 (4.13) and 214 (4.16) nm. IR (KBr): 3435, 3050, 2926, 1646, 1606, and 1255 cm^{-1} . ^1H NMR 7.882 (d, $J = 8.8$ Hz), 6.934 (d, $J = 8.8$ Hz), 6.668 (s), 3.797 (s), 2.394 (s), and 2.163 (s).

Single Crystals Growth

Single crystals adequate for structural X-ray diffraction work were obtained by slow evaporation at room temperature of methanolic solution of sideroxylin. After three days, it was observed the growth of yellow needle-like prismatic crystals.

Single Crystal X-ray Diffraction Data

Crystal data and refinement results for **1** as a monohydrate, $\text{C}_{18}\text{H}_{16}\text{O}_5 \cdot \text{H}_2\text{O}$, are summarized in the Table 1.

Diffraction data were collected at 150K on a KappaCCD diffractometer with COLLECT [11]



and reduced with DENZO and SCALEPACK [12]. In part because of its small scattering volume the crystal diffracted poorly. Only about 54% of the reflection intensities were above two times the standard deviations of experimental errors. The structure was solved by direct and Fourier methods with SHELXS [13] program and its non-H atoms refined anisotropically by full-matrix least-squares with SHELXL [14] program. The hydrogen atoms were positioned stereo-chemically and refined with the riding model. The oxydryl and methyl hydrogen positions were optimized by treating the groups as rigid and allowing them to rotate during the refinement around the corresponding C-O and C-C bonds. The water H-atoms could not be determined reliably and therefore they were not included in the final molecular model.

Atomic fractional coordinates and equivalent isotropic displacement parameters, anisotropic displacement parameters and hydrogen positions are given as supporting information. The structure has been deposited with the Cambridge Crystallographic Data Centre, reference number CCDC-641725.

Antimicrobial Activity

Antimicrobial assays were performed using the agar diffusion methods [15]. The species used in this study were *Candida tropicalis*, *Candida albicans*, *Candida guilliermondii*, *Candida krusei*, and *Candida glabrata* which were recovered from clinical samples.

Microorganisms were grown in Sabouraud agar (Laboratories Britania, Argentina) at 28°C for 48 hours and re-suspended in sterile physiological saline solution with reference to the value 0.5 of the McFarland scale (1.5×10^8 CFU/ml). Petri dishes were prepared with a base layer of Sabouraud agar (10 ml) and wells (6mm of diameter) were made on the surface of the medium. 25 μ l of ethyl acetate extracts with different concentrations along with the pure compound (sideroxylin) were placed in the wells. Nistatine (0, 25 mg/ml) was used as standard.

Microorganisms were incubated at 28°C aerobically and after 48 hrs of incubation the extension of the inhibition zones was measured. Fungal growth inhibition was determined as the diameter of the inhibition zones around the wells. The growth inhibition diameter was the average of four measurements taken along four different directions. Minimal inhibitory concentration (MIC) values were determined by conventional agar plate dilution methods [16]. All tests were performed by triplicate. Inhibition zone diameters

and MIC values for ethyl acetate extract and sideroxylin are showed in Table 2 and 3, respectively.

Results and discussion

Crystal Structure

Figure 2 is an ORTEP [17] plot of the sideroxylin molecule.

Intra-molecular bond distances and angles are listed in Table 4.

The fused rings group is planar [rms deviation of atoms from the best least-squares plane of 0.018 Å]. The phenyl ring attached to this group through a σ -bond is nearly coplanar with it [dihedral angle of 4.37(7)°]. As expected, intra-molecular bond distances within the phenyl rings correspond to a resonance bond structure [C-C bond lengths in the range from 1.380(4) to 1.409(4) Å]. Within the fused hetero-cycle ring, the formally C2-C3 double bond distance is 1.359(4) Å, significantly shorter than formally single C4-C10 and C3-C4 bonds [1.451(4) and 1.409(4) Å, respectively]. Carbonyl C=O distance is 1.271(3) Å, single C(ph)-OH bond lengths are 1.358(3) and 1.360(3) Å, hetero-cycle ring C-O lengths are 1.362(3) and 1.379(3) Å and C(ph)-OCH₃ and O-CH₃ distances are 1.387(3) and 1.445(3) Å, respectively. The fused cycles group presents a strong intra-molecular O-H...O bond [d(O5...O4)=2.604 Å, \angle (O5-H5...O4)=147.0°].

Solid State IR Absorption and Solution NMR and UV Spectra

The IR spectrum of **1** as a solid (in KBr disks) showed bands at 3435, 3050, 2926, 1646, 1606, and 1255 cm^{-1} which correspond to vibrations of a flavonoid skeleton. The presence of this structural group was confirmed by the UV spectrum (carried out in methanol solution 5×10^{-4} M) which showed three bands at λ 328, 279, and 214 nm. Moreover, the assays with shifting reagent [18] showed the following results: with NaOMe they displayed a band I bathochromic shift of 64 nm without decreasing of intensity, a fact indicating the presence of a free 4'-OH. The spectrum with AlCl₃ showed a bathochromic shift of all bands, without recovering original spectrum after addition of HCl, which is indicative of a free 5-OH group. After addition of NaOAc, the spectrum did not showed significant changes when compared with that in MeOH. This fact and that observed on addition of H₃BO₃ indicated the absence of 7-OH and ortho-dihydroxyl groups.

On the other hand, ¹H NMR spectrum, carried out in CD₃OD, showed two d at δ 7.882 ($J = 8.8$



Hz) y 6.934 ($J = 8.8$ Hz) for two protons each which is indicating the presence of the couples H-2',6' and H-3',5'. A singlet at δ 6.668 was assigned to H-3. No signal for A-ring protons was observed. On the other hand, three singlets were observed at δ 3.797, 2.394, and 2.163 which were assigned to the methoxyl group at C-7 and the methyl groups at C-6 and C-8 [9,19].

Based on their UV, ^1H NMR spectra, it can be concluded that the compound **1** detected in solution is the same 4H-1-Benzopyran-4-one, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl (sideroxylin) found in the solid state. The above spectral assignments were further confirmed by comparison with literature data [20].

Antimicrobial Activity

The ethyl acetate extract of *M. ioneura* leaves and the **1** compound purified from it were screened for antifungal activity using *Candida tropicalis*, *C. albicans*, *C. guilliermondii*, *C. krusei*, and *C. glabrata*, which were recovered from clinical samples. From the MIC values listed in Table 2 and 3 we can appreciate that the more potent antifungal activity of both extract and pure **1** were against *C. krusei* followed by *C. guilliermondii* and *C. albicans*. On the other hand, *C. glabrata* showed no inhibition with the assayed concentrations, while *C. tropicalis* showed some inhibition but was not possible to determine the MIC values.

Conclusions

We solved the solid state molecular structure of sideroxylin by single crystal X-ray diffraction methods and characterized its vibration spectrum by IR absorption. The compound was further characterized in solution by NMR and UV spectroscopic techniques.

The antifungal activity observed for sideroxylin are very similar to those observed for the ethyl acetate extract hence indicating that is, the main responsible of biological activity.

The preliminary results presented here may stimulate further studies which could pave the way for the therapeutic use of *M. ioneura* as an antifungal product

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Supplementary Material Available

Listings of atomic fractional coordinates and equivalent isotropic displacement parameters (Table S5), anisotropic displacement parameters for the non-H atoms (Table S6) and hydrogen atoms positions (Table S7).

Note: Part of this study was presented at the 'II Reunión de Biotecnología aplicada a plantas medicinales y aromáticas' (Second Biotechnology Meeting on Medicinal and Aromatic Plants), Córdoba, Argentina, 2009.

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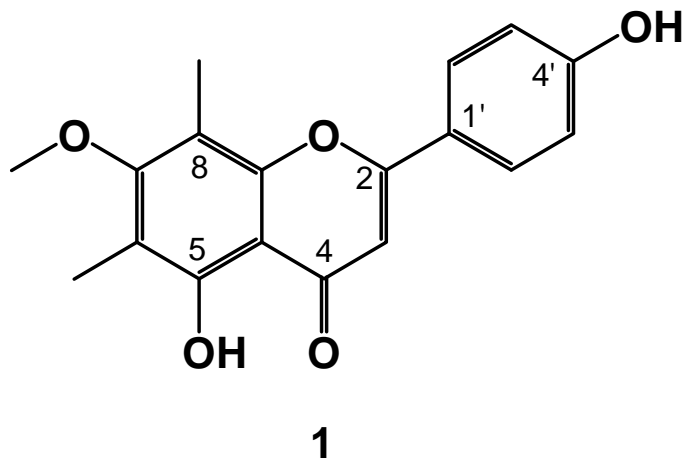


Figure 1: 4H-1-Benzopyran-4-one, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl. (sideroxylin)

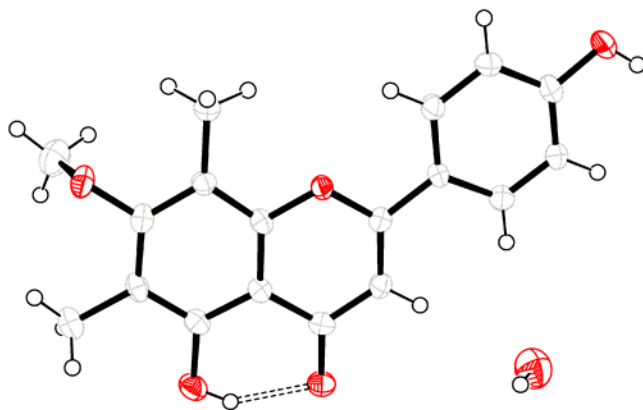


Figure 2. Molecular plot of 4H-1-Benzopyran-4-one, 5-hydroxy-2-(4-hydroxyphenyl)-7-methoxy-6,8-dimethyl showing the labeling of the non-H atoms and their displacement ellipsoids at the 50% probability level. The intra-molecular H-bond is indicated by dashed lines.

**Table 1.** Crystal data and structure solution methods and refinement results for sideroxylin monohydrate.

| | |
|--|---|
| Empirical formula | C ₁₈ H ₁₈ O ₆ |
| Formula weight | 330.32 |
| Temperature (K) | 150(2) |
| Crystal system, space group | monoclinic, P2 ₁ /c |
| Unit cell dimensions ^a | a= 7.322(1) Å b=17.014(2) Å c=12.210(1) Å β=93.73(1)° |
| Volume | 1517.9(3) Å ³ |
| Z, calculated density | 4, 1.446 Mg/m ³ |
| Absorpt. coeff. (μ) | 0.109 mm ⁻¹ |
| F(000) | 696 |
| Crystal size | 0.20 x 0.04 x 0.03 mm ³ |
| Crystal color/shape | yellow/prismatic needle |
| Radiation | graphite monochr. MoKα (λ=0.71073 Å) |
| θ range for data collection | 2.92 to 26.00° |
| Index ranges | -9≤h≤9, -20≤k≤20, -14≤l≤15 |
| Reflections collected/unique | 7925/2948 [R(int)=0.0735] |
| Completeness | 99.5% (to θ=26.00°) |
| Observed reflections[I>2(I)] | 1585 |
| Refinement method | Full-matrix least-squares on F ² |
| Weights, w | [σ ² (F _o ²)+(0.089P) ²] ⁻¹ P=[Max(F _o ² ,0)+2F _c ²]/3 |
| Data/restraints/parameters | 2948/0/220 |
| Goodness-of-fit on F ² | 0.917 |
| Final R indices ^b [I>2σ(I)] | R1=0.0573, wR2=0.1343 |
| R indices (all data) | R1=0.1223, wR2=0.1667 |
| Largest peak and hole | 0.293 and -0.276 e.Å ⁻³ |

^a Least-squares refinement of angular settings for 7925 reflections in the 2.92<θ<26.00° range.

^b R indices defined as: $R1 = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|}$, $wR2 = \frac{\sum w(F_o^2 - F_c^2)^2}{\sum w(F_o^2)^2}^{1/2}$.

Table 2: Minimum Inhibiting Concentrations (MIC) of the ethyl acetate extract of *Miconia ioneura*

| Microorganisms | <i>Candida albicans</i> | <i>Candida krusei</i> | <i>Candida guilliermondii</i> | <i>Candida tropicalis</i> | <i>Candida glabrata</i> |
|---|-------------------------|-----------------------|-------------------------------|---------------------------|-------------------------|
| Growth inhibition diameter (mm) | 12 | 14 | 14 | 8 | .* |
| MIC mg/ml | 0.245 | 0.039 | 0.245 | .* | .* |
| Nistatine growth inhibition diameter (mm) | 24 | 30 | 28 | 24 | 24 |

**Table 3:** Minimum Inhibiting concentration (MIC) of SIDEROXYLYN

| Microorganisms | <i>Candida albicans</i> | <i>Candida krusei</i> | <i>Candida guilliermondii</i> | <i>Candida tropicalis</i> | <i>Candida glabrata</i> |
|---|-------------------------|-----------------------|-------------------------------|---------------------------|-------------------------|
| Growth inhibition diameter (mm) | 10 | 15 | 12 | 12 | -* |
| MIC mg/ml | 0.245 | 0.031 | 0.201 | -* | -* |
| Nistatine growth inhibition diameter (mm) | 24 | 30 | 28 | 24 | 24 |

*(-) non inhibition

Table 4. Intra-molecular bond distances (Å) and angles (°) for sideroxylin monohydrate.

| Bond distances | | | |
|-----------------|----------|-------------------|----------|
| O(1)-C(2) | 1.362(3) | C(6)-C(7) | 1.393(4) |
| O(1)-C(9) | 1.379(3) | C(6)-C(11) | 1.509(4) |
| O(4)-C(4) | 1.271(3) | C(7)-C(8) | 1.405(4) |
| O(5)-C(5) | 1.358(3) | C(8)-C(9) | 1.383(4) |
| O(7)-C(7) | 1.387(3) | C(8)-C(13) | 1.506(4) |
| O(7)-C(12) | 1.445(4) | C(9)-C(10) | 1.396(4) |
| O(4')-C(4') | 1.360(3) | C(1')-C(2') | 1.395(4) |
| C(2)-C(3) | 1.359(4) | C(1')-C(6') | 1.402(4) |
| C(2)-C(1') | 1.463(4) | C(2')-C(3') | 1.386(4) |
| C(3)-C(4) | 1.409(4) | C(3')-C(4') | 1.396(4) |
| C(4)-C(10) | 1.451(4) | C(4')-C(5') | 1.387(4) |
| C(5)-C(6) | 1.392(4) | C(5')-C(6') | 1.380(4) |
| C(5)-C(10) | 1.409(4) | | |
| Bond angles | | | |
| C(2)-O(1)-C(9) | 120.8(2) | C(9)-C(8)-C(13) | 122.1(3) |
| C(7)-O(7)-C(12) | 113.3(2) | C(7)-C(8)-C(13) | 122.5(2) |
| C(3)-C(2)-O(1) | 120.9(3) | O(1)-C(9)-C(8) | 115.9(2) |
| C(3)-C(2)-C(1') | 127.1(2) | O(1)-C(9)-C(10) | 120.4(2) |
| O(1)-C(2)-C(1') | 112.1(2) | C(8)-C(9)-C(10) | 123.7(3) |
| C(2)-C(3)-C(4) | 121.9(3) | C(9)-C(10)-C(5) | 117.9(2) |
| O(4)-C(4)-C(3) | 122.9(3) | C(9)-C(10)-C(4) | 119.3(3) |
| O(4)-C(4)-C(10) | 120.5(3) | C(5)-C(10)-C(4) | 122.8(3) |
| C(3)-C(4)-C(10) | 116.6(3) | C(2')-C(1')-C(6') | 118.1(3) |
| O(5)-C(5)-C(6) | 117.9(3) | C(2')-C(1')-C(2) | 121.3(2) |
| O(5)-C(5)-C(10) | 120.7(2) | C(6')-C(1')-C(2) | 120.6(3) |
| C(6)-C(5)-C(10) | 121.4(3) | C(3')-C(2')-C(1') | 121.4(3) |
| C(5)-C(6)-C(7) | 117.2(3) | C(2')-C(3')-C(4') | 119.5(3) |
| C(5)-C(6)-C(11) | 119.8(3) | O(4')-C(4')-C(5') | 122.8(3) |
| C(7)-C(6)-C(11) | 123.0(3) | O(4')-C(4')-C(3') | 117.5(3) |
| O(7)-C(7)-C(6) | 118.8(3) | C(5')-C(4')-C(3') | 119.7(3) |
| O(7)-C(7)-C(8) | 116.9(3) | C(6')-C(5')-C(4') | 120.4(3) |
| C(6)-C(7)-C(8) | 124.3(2) | C(5')-C(6')-C(1') | 120.8(3) |
| C(9)-C(8)-C(7) | 115.4(3) | | |



Table S5. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for sideroxylin monohydrate. $U(\text{eq})$ for the non-H atoms is defined as one third of the trace of the orthogonalized U_{ij} tensor.

| Atom | x | y | z | U (eq) |
|-------|----------|----------|---------|--------|
| O(1) | 2356(3) | 657(1) | 5591(1) | 24(1) |
| O(4) | 2700(3) | -1248(1) | 3590(2) | 32(1) |
| O(5) | 4241(3) | -2035(1) | 5231(2) | 35(1) |
| O(7) | 4979(3) | -717(1) | 8659(2) | 34(1) |
| O(4') | -1130(3) | 3690(1) | 3447(2) | 36(1) |
| C(2) | 1723(4) | 699(2) | 4518(2) | 22(1) |
| C(3) | 1808(4) | 66(2) | 3844(2) | 26(1) |
| C(4) | 2583(4) | -653(2) | 4211(2) | 26(1) |
| C(5) | 4036(4) | -1375(2) | 5837(2) | 26(1) |
| C(6) | 4605(4) | -1400(2) | 6947(2) | 27(1) |
| C(7) | 4373(4) | -721(2) | 7559(2) | 26(1) |
| C(8) | 3618(4) | -18(2) | 7129(2) | 25(1) |
| C(9) | 3086(4) | -32(2) | 6022(2) | 22(1) |
| C(10) | 3251(4) | -692(2) | 5355(2) | 23(1) |
| C(11) | 5428(4) | -2145(2) | 7435(3) | 34(1) |
| C(12) | 3650(5) | -1024(2) | 9372(3) | 50(1) |
| C(13) | 3415(5) | 705(2) | 7821(2) | 34(1) |
| C(1') | 997(4) | 1478(2) | 4229(2) | 23(1) |
| C(2') | 1079(4) | 2093(2) | 4988(2) | 30(1) |
| C(3') | 383(4) | 2830(2) | 4718(2) | 33(1) |
| C(4') | -424(4) | 2963(2) | 3667(2) | 29(1) |
| C(5') | -478(4) | 2363(2) | 2897(2) | 27(1) |
| C(6') | 215(4) | 1630(2) | 3172(2) | 26(1) |
| O(1W) | 1126(4) | 376(2) | 1013(2) | 64(1) |

**Table S6.** Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for sideroxylin monohydrate. The anisotropic displacement factor exponent takes the form: $-2\pi^2(h^2a^*U_{11} + \dots + 2hka^*b^*U_{12})$. To be deposited.

| Atom | U11 | U22 | U33 | U23 | U13 | U12 |
|-------|-------|-------|-------|-------|-------|-------|
| O(1) | 28(1) | 20(1) | 23(1) | 1(1) | -2(1) | |
| 1(1) | | | | | | |
| O(4) | 40(1) | 25(1) | 31(1) | -5(1) | -1(1) | - |
| 2(1) | | | | | | |
| O(5) | 41(1) | 24(1) | 39(1) | -4(1) | -4(1) | |
| 4(1) | | | | | | |
| O(7) | 37(1) | 37(1) | 25(1) | 6(1) | -6(1) | - |
| 1(1) | | | | | | |
| O(4') | 48(1) | 24(1) | 36(1) | 2(1) | -5(1) | 10(1) |
| C(2) | 22(2) | 23(2) | 23(1) | 1(1) | 1(1) | - |
| 4(1) | | | | | | |
| C(3) | 25(2) | 29(2) | 22(1) | 1(1) | -1(1) | 0(1) |
| C(4) | 23(2) | 24(2) | 30(2) | -3(1) | 3(1) | - |
| 1(1) | | | | | | |
| C(5) | 25(2) | 20(2) | 33(2) | 1(1) | 3(1) | - |
| 5(1) | | | | | | |
| C(6) | 25(2) | 22(2) | 35(2) | 9(1) | 0(1) | - |
| 2(1) | | | | | | |
| C(7) | 24(2) | 29(2) | 26(1) | 5(1) | -1(1) | - |
| 3(1) | | | | | | |
| C(8) | 26(2) | 23(2) | 26(1) | -2(1) | 0(1) | - |
| 1(1) | | | | | | |
| C(9) | 19(2) | 18(2) | 29(1) | 3(1) | 1(1) | - |
| 3(1) | | | | | | |
| C(10) | 20(2) | 20(2) | 28(2) | 1(1) | 1(1) | - |
| 3(1) | | | | | | |
| C(11) | 33(2) | 27(2) | 42(2) | 9(2) | -2(1) | 1(2) |
| C(12) | 58(3) | 54(3) | 37(2) | 10(2) | 4(2) | - |
| 5(2) | | | | | | |
| C(13) | 44(2) | 27(2) | 30(2) | -2(1) | -3(1) | 2(2) |
| C(1') | 22(2) | 21(2) | 25(1) | 3(1) | 0(1) | 1(1) |
| C(2') | 36(2) | 25(2) | 27(2) | 1(1) | -7(1) | 1(1) |
| C(3') | 43(2) | 26(2) | 30(2) | -5(1) | -2(1) | 2(2) |
| C(4') | 28(2) | 24(2) | 34(2) | 7(1) | 3(1) | |
| 2(1) | | | | | | |
| C(5') | 28(2) | 28(2) | 26(1) | 3(1) | -2(1) | |
| 2(1) | | | | | | |
| C(6') | 26(2) | 24(2) | 28(1) | -1(1) | -1(1) | - |
| 4(1) | | | | | | |
| O(1W) | 67(2) | 61(2) | 62(2) | 4(2) | -2(1) | |
| 4(2) | | | | | | |

**Table S7.** Hydrogen coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for sideroxylin monohydrate.

| Atom | x | y | z | U(eq) |
|--------|-------|-------|-------|-------|
| H(5) | 3869 | -1951 | 4594 | 42 |
| H(4') | -1526 | 3709 | 2804 | 44 |
| H(3) | 1331 | 109 | 3104 | 31 |
| H(11A) | 6077 | -2026 | 8143 | 52 |
| H(11B) | 6290 | -2366 | 6936 | 52 |
| H(11C) | 4454 | -2526 | 7543 | 52 |
| H(12A) | 2487 | -744 | 9235 | 75 |
| H(12B) | 4097 | -951 | 10139 | 75 |
| H(12C) | 3464 | -1586 | 9225 | 75 |
| H(13A) | 4555 | 1008 | 7848 | 51 |
| H(13B) | 3146 | 550 | 8566 | 51 |
| H(13C) | 2410 | 1029 | 7499 | 51 |
| H(2') | 1624 | 2003 | 5704 | 36 |
| H(3') | 454 | 3242 | 5245 | 40 |
| H(5') | -996 | 2457 | 2175 | 33 |
| H(6') | 160 | 1223 | 2638 | 31 |