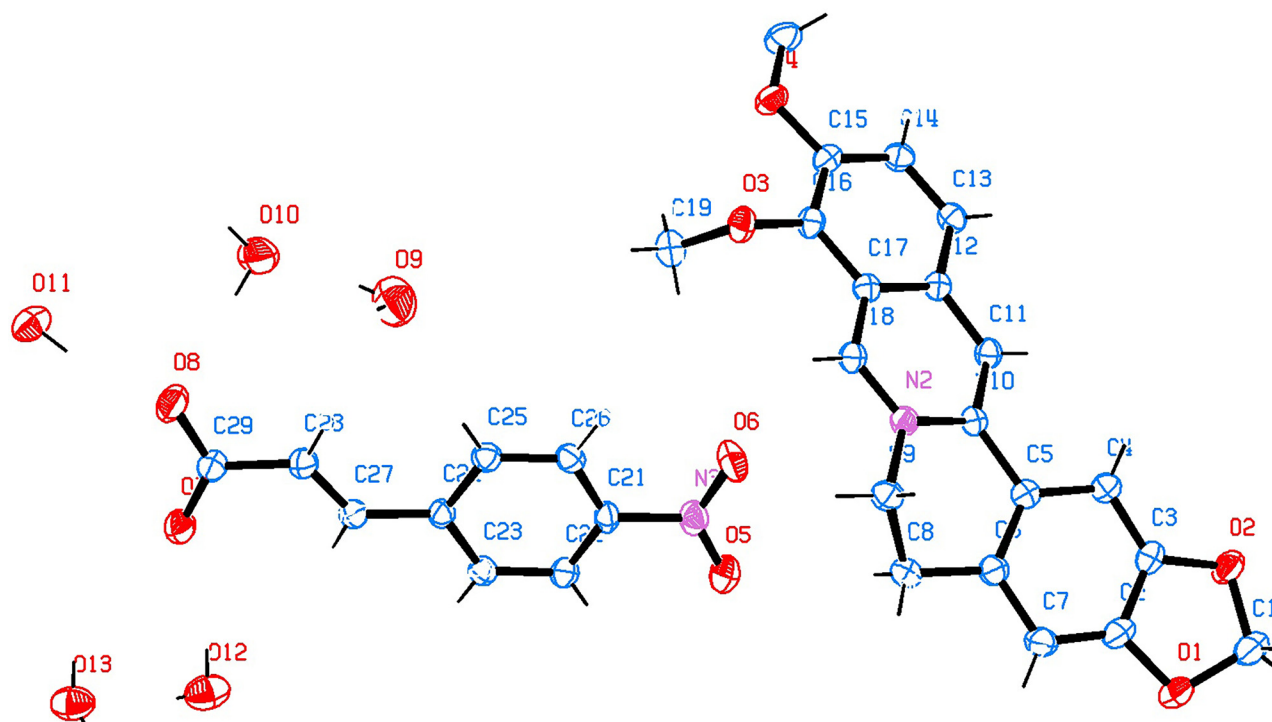


Shi-Yun Chen, Wei Wang, Yong He* and Deng-ke Yin

The crystal structure of 9,10-dimethoxy-5,6-dihydro-[1,3]dioxolo[4,5-*g*]isoquinolino [3,2-*a*]isoquinolin-7-ium (*E*)-3-(4-nitrophenyl)acrylate pentahydrate, C₂₉H₃₄N₂O₁₃



<https://doi.org/10.1515/ncrs-2023-0331>

Received July 18, 2023; accepted August 21, 2023;

published online September 6, 2023

$\gamma = 90.247(1)^\circ$, $V = 1437.00(6) \text{ \AA}^3$, $Z = 2$, $R_{gt}(F) = 0.0457$, $wR_{ref}(F^2) = 0.1218$, $T = 193 \text{ K}$.

CCDC no.: 2252770

Abstract

C₂₉H₃₄N₂O₁₃, triclinic, $P\bar{1}$ (no. 2), $a = 8.1996(2) \text{ \AA}$, $b = 13.1993(3) \text{ \AA}$, $c = 13.5119(3) \text{ \AA}$, $\alpha = 94.208(1)^\circ$, $\beta = 99.787(1)^\circ$,

Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

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1 Source of materials

Berberine sulfate (hydrate) (0.86 g, 2 mmol) was dissolved in water (50 mL) at 50 °C to obtain a clear solution. A solution of NaOH (0.08 g, 2 mmol) and 4-nitro-cinnamic acid (PNCA) (0.38 g, 2 mmol) in water (20 mL) were added. The mixture was heated to 50 °C to get a brown coloured solution. Crystals

Table 1: Data collection and handling.

Crystal:	Brown block
Size:	0.13 × 0.12 × 0.10 mm
Wavelength:	Ga K α radiation (1.34139 Å)
μ :	0.61 mm ⁻¹
Diffractometer, scan mode:	Bruker D8 VENTURE PHOTON II, φ and ω
$\theta_{\max}$, completeness:	60.3°, %
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	13,791, 6231, 0.043
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 4466
$N(\text{param})_{\text{refined}}$:	217
Programs:	Bruker [1], SHELX [2, 3]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C1	0.6625 (2)	0.40911 (15)	1.46588 (13)	0.0412 (4)
H1A	0.747871	0.444740	1.517461	0.049*
H1B	0.586977	0.371344	1.500452	0.049*
C2	0.6403 (2)	0.34556 (13)	1.30742 (12)	0.0306 (4)
C3	0.5421 (2)	0.43061 (12)	1.30916 (12)	0.0284 (4)
C4	0.43528 (19)	0.45607 (12)	1.22622 (12)	0.0270 (4)
H4	0.369421	0.515013	1.227851	0.032*
C5	0.42706 (19)	0.39111 (11)	1.13817 (12)	0.0251 (3)
C6	0.52366 (19)	0.30398 (12)	1.13722 (12)	0.0274 (4)
C7	0.6338 (2)	0.28074 (13)	1.22376 (13)	0.0315 (4)
H7	0.700907	0.222242	1.223845	0.038*
C8	0.5055 (2)	0.23647 (12)	1.04141 (13)	0.0330 (4)
H8A	0.540452	0.166848	1.056801	0.040*
H8B	0.577267	0.262328	0.996564	0.040*
C9	0.3276 (2)	0.23416 (11)	0.98930 (13)	0.0304 (4)
H9A	0.316687	0.192185	0.924650	0.037*
H9B	0.257110	0.203051	1.031915	0.037*
C10	0.31815 (19)	0.41631 (11)	1.04520 (11)	0.0238 (3)
C11	0.26007 (19)	0.51182 (11)	1.02772 (12)	0.0253 (3)
H11	0.291059	0.565790	1.078011	0.030*
C12	0.15580 (18)	0.53236 (11)	0.93742 (11)	0.0234 (3)
C13	0.09069 (19)	0.62873 (12)	0.91769 (12)	0.0270 (4)
H13	0.112214	0.683439	0.968104	0.032*
C14	−0.00325 (19)	0.64415 (12)	0.82653 (12)	0.0279 (4)
H14	−0.045617	0.709768	0.814243	0.033*
C15	−0.03842 (19)	0.56429 (12)	0.75035 (12)	0.0265 (3)
C16	0.01737 (19)	0.46816 (11)	0.76812 (12)	0.0254 (3)
C17	0.11489 (18)	0.45095 (11)	0.86228 (11)	0.0237 (3)
C18	0.17555 (19)	0.3546 (11)	0.88341 (12)	0.0253 (3)
H18	0.147483	0.299175	0.834481	0.030*
C19	0.0734 (2)	0.38137 (14)	0.61956 (13)	0.0399 (4)
H19A	0.039269	0.321176	0.573711	0.060*
H19B	0.190719	0.376514	0.648847	0.060*
H19C	0.056803	0.442436	0.582190	0.060*
C20	−0.1790 (2)	0.67549 (13)	0.63255 (14)	0.0396 (4)
H20A	−0.244978	0.672231	0.564698	0.059*
H20B	−0.080289	0.718245	0.634678	0.059*
H20C	−0.245318	0.704600	0.681145	0.059*
C21	0.5776 (2)	0.21634 (11)	0.66085 (11)	0.0267 (4)
C22	0.7251 (2)	0.19164 (12)	0.62999 (12)	0.0293 (4)

Table 2: (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
H22	0.827770	0.206847	0.673009	0.035*
C23	0.7197 (2)	0.14409 (12)	0.53465 (12)	0.0287 (4)
H23	0.820046	0.127074	0.511580	0.034*
C24	0.56855 (19)	0.12092 (11)	0.47211 (11)	0.0250 (3)
C25	0.4213 (2)	0.14556 (11)	0.50737 (12)	0.0272 (4)
H25	0.317842	0.128657	0.465831	0.033*
C26	0.4251 (2)	0.19401 (11)	0.60161 (12)	0.0273 (4)
H26	0.325478	0.211620	0.625287	0.033*
C27	0.5693 (2)	0.06989 (12)	0.37173 (12)	0.0269 (3)
H27	0.674421	0.056009	0.353619	0.032*
C28	0.4377 (2)	0.04150 (12)	0.30429 (12)	0.0292 (4)
H28	0.331429	0.053183	0.321511	0.035*
C29	0.4472 (2)	−0.00769 (12)	0.20301 (12)	0.0288 (4)
N2	0.27136 (16)	0.33904 (9)	0.97017 (9)	0.0242 (3)
N3	0.58185 (19)	0.26806 (10)	0.76089 (11)	0.0332 (3)
O1	0.73853 (15)	0.34079 (10)	1.40050 (9)	0.0391 (3)
O2	0.57185 (15)	0.48065 (9)	1.40372 (8)	0.0373 (3)
O3	−0.02383 (14)	0.38722 (8)	0.69845 (8)	0.0309 (3)
O4	−0.12997 (14)	0.57516 (8)	0.65761 (8)	0.0331 (3)
O5	0.71451 (18)	0.27646 (11)	0.81835 (10)	0.0506 (4)
O6	0.45331 (17)	0.30309 (10)	0.78304 (10)	0.0456 (3)
O7	0.58137 (15)	−0.04250 (10)	0.18472 (9)	0.0405 (3)
O8	0.31460 (15)	−0.01130 (10)	0.13977 (9)	0.0433 (3)
O9	0.0204 (2)	0.07935 (13)	0.37249 (12)	0.0627 (4)
H9C	0.025552	0.094081	0.311390	0.094*
H9D	−0.015205	0.016615	0.365972	0.094*
O10	0.06230 (18)	0.12005 (10)	0.17255 (12)	0.0526 (4)
H10A	0.141171	0.078422	0.163261	0.079*
H10B	−0.023277	0.096687	0.129675	0.079*
O11	0.21619 (15)	−0.01936 (10)	−0.05997 (9)	0.0407 (3)
H11A	0.263852	−0.020782	0.002549	0.061*
H11B	0.295529	−0.003191	−0.091552	0.061*
O12	0.87790 (16)	−0.12151 (11)	0.28528 (11)	0.0495 (4)
H12A	0.786091	−0.091699	0.262688	0.074*
H12B	0.935291	−0.120417	0.236799	0.074*
O13	1.01618 (16)	−0.13927 (10)	0.10689 (11)	0.0481 (4)
H13A	1.116802	−0.114675	0.118380	0.072*
H13B	0.956934	−0.091730	0.077932	0.072*

of the title compound were obtained by slow evaporation within 4 days.

2 Experimental details

Data collection was performed on a Bruker D8 VENTURE Metaljet PHOTON II diffractometer at 193 K, operating at 50 kV and 30 mA. Data were processed by the BRUKER AXS Crystal Structure Analysis Package [1]. Data collection, BRUKER APEX3; cell refinement and data reduction by BRUKER SAINT V8.40B; Structure solution: SHELXT 2014/5 [2]; Structure refinement: SHELXL-2018/3 [3]; Molecular graphics and publication materials by BRUKER SHELXTL [2]. All

H-atoms were placed geometrically and refined using a riding model with common isotropic displacement factors, U_{iso} values were set to $1.2U_{eq}$ of the parent atoms.

3 Comment

Berberine hydrochloride (BBR-HCl) is contained in the Chinese Pharmacopoeia (2020) for gastrointestinal infections such as gastroenteritis and bacillary dysentery caused by sensitive pathogens. But, it presents poor intestine absorption *via* oral administration. Additionally, BBR-HCl is highly hygroscopic and presents an extremely bitter taste. Cocrystals have been prepared in attempts to solve these problems. Recently, A wide range of cofomers, such as flavonoids (myricetin, dihydromyricetin [4], chrysin [5]); anthraquinones (emodin [6], rhein [7]); API (Ibuprofen [8], rosiglitazone [9, 10]), aromatic carboxylic [11] (3,4,5-methoxycinnamic acid [12], carboxylic acids [13]) and small molecular organic acid (aliphatic dicarboxylic acids [14], L(+)-lactic acid [15]) can be if hydrogen bonding formation is possible, providing many options to develop pharmaceutical products with improved pharmaceutical properties, including solubility.

It is worth noting that, by reacting Berberine sulfate and ((4-nitrophenyl) acrylic acid) via a liquid phase reaction, the title salt has been obtained. The asymmetric unit of the title structure contains one 9,10-dimethoxy-5,6-dihydro-[1, 3] dioxolo[4,5-g]isoquinolino [3,2-a]isoquinolin-7-ium cation, one (*E*)-3-(4-nitrophenyl) acrylate anion and five water molecules. All moieties are connected by hydrogen bonds. All bond lengths are in the expected ranges. The proportions of lattice water in each crystal lattice account for 14.5%. The cavity can be clearly observed when the lattice waters were removed from the crystal lattice, which plays a critical role in supporting the three dimensional structures. This means lattice water is an important hydrogen donor acceptor in the title salt.

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: We gratefully acknowledge support by The Key project of Anhui Provincial Department of Education, China (NO. KJ2020A672 and 2022AH040077) and The Open Fund Project of Anhui Key Laboratory of Pharmaceutical Preparation Technology and Application (NO. 2021KFKT08).

Co-authors would like to thank Zhang CX from Shiyanjia Lab (www.shiyanjia.com) for the SXRD analysis.

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