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Berberine formate–succinic acid (1/1)

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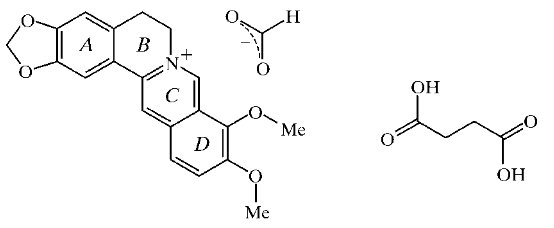
The title compound [systematic name: 9,10-dimethoxy-2,3-methylenedioxy-5,6-dihydrodibenzo[*a*,*g*]quinolizinium formate–succinic acid (1/1)], $C_{20}H_{18}NO_4^+\cdot CHO_2^-\cdot C_4H_6O_4$, contains centrosymmetric pairs of almost planar berberine cations, and hydrogen-bonded $(C_4H_6O_4\cdots HCOO^-)_2$ rings of succinic acid with formate anions, bonded by O—H···O hydrogen bonds with O···O distances of 2.4886 (15) and 2.5652 (16) Å. Pairs of cations and molecules of succinic acid are connected by non-conventional weak C—H···O hydrogen bonds, with C···O distances of 3.082 (2) and 3.178 (2) Å.

Comment

Berberine (9,10-dimethoxy-2,3-methylenedioxy-5,6-dihydrodibenzo[*a*,*g*]quinolizinium) is an isoquinoline alkaloid of the protoberberine group, which is commonly found in the *Papaveraceae*, *Berberidaceae* and other plant families (Bentley, 1998). Berberine is known as an antimicrobial agent and is used for the treatment of eye infections, gastrointestinal disorders and other diseases (Schmeller & Wink, 1998; Simeon *et al.*, 1989). Recently, its interactions with nucleic acids and cells have been extensively investigated (Mazzini *et al.*, 2003; Slaninová *et al.*, 2001). The berberine skeleton is rather sensitive to nucleophilic attack and 8-substituted-7,8-dihydroberberine derivatives, frequently claimed as genuine natural products, are easily formed (Marek *et al.*, 2003). We report here the first crystal structure of a quaternary protoberberine alkaloid crystallizing with an organic counter-anion to give the title adduct, (I). These organic anions could play a significant role in plant tissues.

The structure of the berberine cation in (I) is similar to that in other berberine salts reported in the literature (Abadi *et al.*, 1984; Kariuki & Jones, 1995; Man *et al.*, 2001). The interplanar angles between aromatic rings *A*/*C*, *A*/*D* and *C*/*D* are 13.36 (5), 13.21 (5) and 1.71 (4)°, respectively. The methoxy group at C10 lies almost in the plane of ring *D* [the deviations of atoms O4 and C16 from this plane are 0.0576 (11) and 0.134 (2) Å, respectively], whereas the methoxy group at C9 is almost perpendicular to the same plane [the C15—O3—C9—C10 torsion angle is −80.8 (2)° and the deviation of atom C15 from the plane of ring *D* is 1.147 (2) Å].



(I)

The berberine units are arranged in centrosymmetric pairs with face-to-face geometry similar to that of norchelerythrine (Marek *et al.*, 2002), forming columns parallel to the crystallographic *a* axis. The packing slip is probably formed in order to optimize *σ*–*π* and *π*–*π* stacking interactions (Hunter & Sanders, 1990). The formate anions and flexible succinic acid molecules fill up the space between these columns. Pairs of berberine cations and $(C_4H_6O_4\cdots HCOO^-)_2$ hydrogen-bonded rings are held together by several C—H···O contacts. The C—H···O interatomic distances for atoms H8 and H13 are rather short [H···O = 2.27 (2) and 2.26 (2) Å, respectively] and should be classified as non-conventional weak hydrogen bonds rather than van der Waals contacts (Steiner & Desiraju, 1998; Desiraju & Steiner, 1999). This classification is supported by their bond directionalities [161.3 (15) and

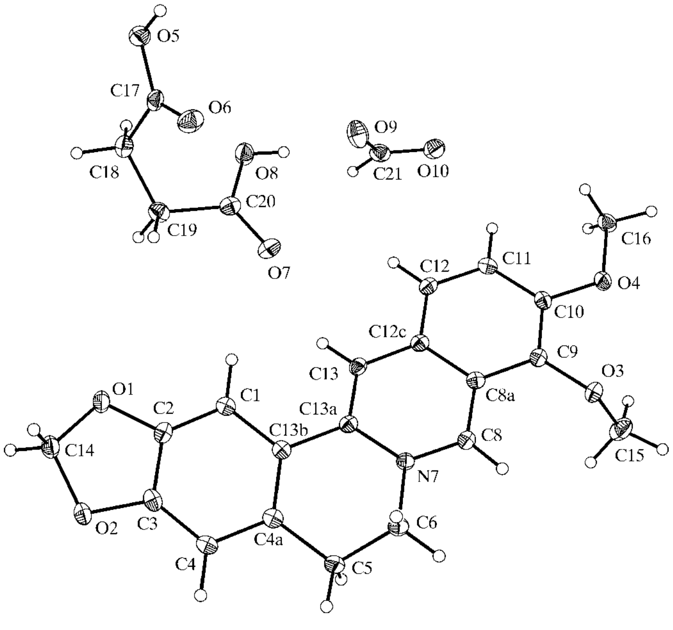


Figure 1
A view of the three components of (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

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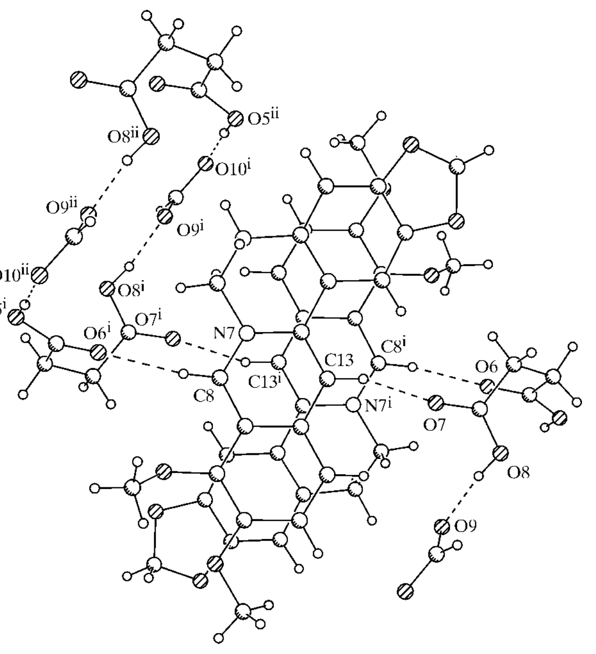

Figure 2
Part of the crystal structure of (I), showing the standard and non-conventional hydrogen-bonding networks. [Symmetry codes: (i): $-x$, $-y$, $-z$; (ii): $-x$, $-y-1$, $-z$.]

148 (2)°, respectively] and assumed binding energies (Cannizzaro & Houk, 2002). We attribute these rather short C8—H8···O and C13—H13···O hydrogen bonds found in the crystal structure of (I) to the felicitous confluence of the pronounced electron-acceptor properties of cationic berberine and the electron-donor properties of the anionic hydrogen-bonded $(C_4H_6O_4\cdots HCOO^-)_2$ macrocycle (Fig. 2 and Table 2).

Experimental

The title compound was obtained by decomposition of 8-(imidazol-1-yl)-7,8-dihydroberberine and crystallization from undistilled tetrahydrofuran.

Crystal data

$C_{20}H_{18}NO_4^+\cdot CHO_2^-\cdot C_4H_6O_4$
$M_r = 499.46$
Triclinic, $P\overline{1}$
$a = 7.9973$ (8) Å
$b = 12.4449$ (9) Å
$c = 12.6115$ (12) Å
$\alpha = 63.753$ (8)°
$\beta = 81.410$ (8)°
$\gamma = 84.866$ (7)°
$V = 1112.74$ (19) Å^3
$Z = 2$
$D_x = 1.491$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 5207 reflections
$\theta = 3.0$–28.4°
$\mu = 0.12$ mm^{-1}
$T = 100$ (2) K
Prism, yellow
0.6 × 0.5 × 0.4 mm

Data collection

Kuma KM-4 diffractometer with a CCD area-detector
Rotation method, ω scans
5978 measured reflections
3802 independent reflections
3443 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.027$
$\theta_{\rm max} = 25°$
$h = -8 \rightarrow 9$
$k = -14 \rightarrow 14$
$l = -14 \rightarrow 13$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.034$
$wR(F^2) = 0.115$
$S = 1.03$
3802 reflections
355 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.075P)^2 + 0.5P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max} = 0.28$ e Å^{-3}
$\Delta\rho_{\rm min} = -0.34$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C2	1.3866 (17)	C4a—C5	1.511 (2)
O1—C14	1.4404 (18)	C5—C6	1.520 (2)
O2—C3	1.3761 (18)	C6—N7	1.4993 (18)
O2—C14	1.4484 (19)	N7—C8	1.3377 (19)
O3—C9	1.3794 (17)	N7—C13a	1.3987 (19)
O3—C15	1.4402 (19)	C8—C8a	1.404 (2)
O4—C10	1.3659 (18)	C8a—C12a	1.430 (2)
O4—C16	1.4437 (18)	C12a—C13	1.408 (2)
C4a—C13b	1.403 (2)	C13a—C13b	1.476 (2)
C9—O3—C15	114.34 (11)	O3—C9—C10	121.65 (13)
C10—O4—C16	117.29 (11)	O3—C9—C8a	118.87 (13)
C8—N7—C13a	122.35 (13)	O4—C10—C9	116.61 (13)
C8—N7—C6	118.18 (12)	O4—C10—C11	123.10 (13)
C13a—N7—C6	119.26 (12)		

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O5—H5···O10$^{\rm i}$	0.84	1.73	2.5652 (16)	176
O8—H8···O9	0.84	1.66	2.4886 (15)	169
C13—H13···O7	0.92 (2)	2.26 (2)	3.0825 (18)	147.9 (16)
C8—H8*A*···O6$^{\rm ii}$	0.943 (19)	2.270 (19)	3.1775 (19)	161.3 (15)

Symmetry codes: (i) $-x$, $-1-y$, $-z$; (ii) $-x$, $-y$, $-z$.

All H atoms were located in a difference electron-density map. H atoms of methyl, CH_2 and OH groups were fixed in their theoretical geometrical positions, with $U_{\rm eq}$ values equal to $1.5U_{\rm eq}$, $1.2U_{\rm eq}$ and $1.5U_{\rm eq}$ of the attached atoms, respectively. Other H atoms were refined freely [C—H = 0.92 (2)–1.00 (2) Å].

Data collection: *CrysAlisCCD* (Oxford Diffraction, 2002); cell refinement: *CrysAlisRED* (Oxford Diffraction, 2002); data reduction: *CrysAlisRED*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*III (Johnson & Burnett, 1996); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1177). Services for accessing these data are described at the back of the journal.

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