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α-{3-[2-(Dimethylammonio)ethyl]-1*H*-indol-5-yl}-*N*-methylmethanesulfonamide succinate (sumatriptan succinate)

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.004 Å
R factor = 0.064
wR factor = 0.158
Data-to-parameter ratio = 16.6

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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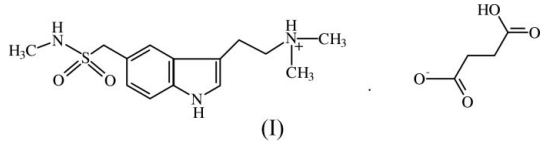
The title compound, $C_{14}H_{22}N_3O_2S^+\cdot C_4H_5O_4^-$, a well known agonist of the 5-hydroxytryptamine receptor, consists of sumatriptan cations and succinate anions. The ten-membered indole ring system is planar. The succinate moiety is nearly perpendicular to the ethylamine side chain, with a (−)synclinal conformation. The structure is stabilized by O—H···O, C—H···O and C—H···π intermolecular interactions.

Comment

A number of serotonin (5-HT) agonists (triptans) are available worldwide for the treatment of migraine. The first-generation triptan, sumatriptan, was the first selective serotonin for the acute treatment of migraine attacks. Its biological and pharmacological aspects have been studied (Evers *et al.*, 2003; Dahlof, 2003; Diener, 2003) but, to our knowledge, the crystal structure has not yet been reported. Bearing in mind its importance, in the light of protein drug binding studies, we report here the crystal structure of the title compound, (I), along with conformational studies. The structure of (I), with the atom numbering scheme, is shown in Fig. 1.



(I)

The indole nucleus is planar, with a maximum deviation from the mean plane of 0.026 (3) Å for atom C7, the dihedral angle between the mean planes of the pyrrole and benzene rings being 1.8 (1)°. The *N*-methylsulfamoyl side chain is folded in such a way that it acquires a −*ac*, *ap* and *sc* conformation, with torsion angles C2—C3—C13—S1 = −93.9 (3)°, C3—C13—S1—N3 = −177.2 (2)° and C13—S1—N3—C14 = 88.1 (3)°, respectively. The position of the α-C atom, C10, in the ethylamine side chain differs significantly [C7—C8—C9—C10 = −112.1 (3)°] from the predicted values of 0, 90 or −90° (Chothia & Pauling, 1969). This is comparable to the literature values (Karle *et al.*, 1965; Falkenberg & Carlstrom, 1971). Dimethylammonium atom N1 shows quarternary character as a result of proton transfer from the succinate moiety ($C_4H_6O_4$) and consequently bears the positive charge in the molecular cation. The bond angles at N1 range from 110.5 (2) to 113.4 (3)°, confirming the tetrahedral configuration. The position of the quarternary N atom relative to the α-C atom gives an *anti* conformation [C8—C9—C10—N1 = −166.9 (2)°]. The plane of the ethylamine side chain (atoms C8, C9, C10, N1 and C11) makes an angle of 72.0 (2)°

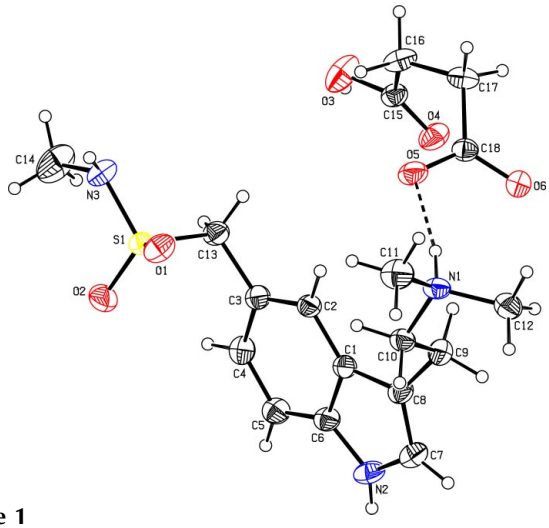


Figure 1
A view of (I), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are represented by circles of arbitrary size. The dashed line indicates the hydrogen bond between the sumatriptan and succinate ions.

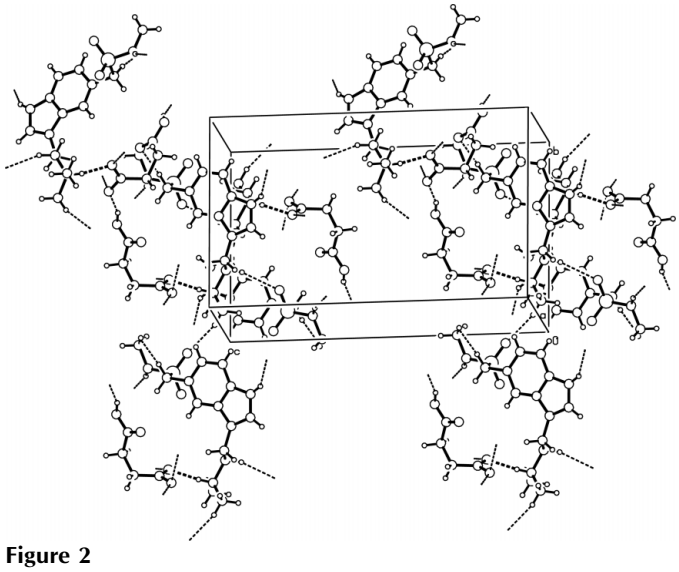


Figure 2
The packing, viewed approximately along the *c* axis. Broken lines indicate hydrogen bonds.

with the plane of the indole ring system. The ethylamine side chain is maximally extended, with a C9—C10—N1—C11 torsion angle of 176.7 (2)°, indicating an antiperiplanar conformation. The C4—C5 bond [1.370 (4) Å] is significantly shorter than the standard C—C bond of benzene [1.397 (1) Å; Lipson & Cochran, 1966]. The succinate anion, with almost equal angles [114.0 (2) and 114.4 (2)°] at atoms C16 and C17, is nearly perpendicular to the ethylamine side chain, with a *−sc* conformation.

The crystal structure contains an extensive hydrogen-bonded network (Table 2). In addition, symmetry-related molecules are also linked by weak C—H···π intermolecular interactions, such that atom H11A is 2.75 Å from the centroid of the benzene ring at $(-x, 1-y, -z)$, with a C11—H11*A*···centroid angle of 131° and a C11···centroid distance of 3.455 (3) Å.

Experimental

The title compound was obtained from S M S Pharma Research Centre, Hyderabad, and was recrystallized from aqueous methanol (1:1).

Crystal data

$C_{14}H_{22}N_3O_2S^+\cdot C_4H_5O_4^-$
M_r = 413.49
Monoclinic, $P2_1/c$
a = 9.9076 (9) Å
b = 11.2342 (10) Å
c = 18.7010 (16) Å
β = 92.602 (2)°
V = 2079.3 (3) Å^3
Z = 4
D_x = 1.321 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2738 reflections
θ = 2.8–23.8°
μ = 0.19 mm^{-1}
T = 293 (2) K
Block, colourless
0.21 × 0.20 × 0.18 mm

Data collection

Bruker SMART APEX CCD area-detector diffractometer
ω scans
12 456 measured reflections
4525 independent reflections
3431 reflections with $I > 2\sigma(I)$
R_{int} = 0.033
θ_{max} = 28.1°
$h = -13 \rightarrow 11$
$k = -14 \rightarrow 14$
$l = -21 \rightarrow 21$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.064
$wR(F^2)$ = 0.158
S = 1.10
4525 reflections
272 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.072P)^2 + 0.603P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.29 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—O2	1.423 (2)	O6—C18	1.254 (3)
S1—O1	1.425 (2)	N1—C12	1.484 (4)
S1—N3	1.601 (2)	N1—C11	1.487 (4)
S1—C13	1.779 (3)	N1—C10	1.493 (3)
O3—C15	1.304 (3)	N2—C7	1.358 (4)
O4—C15	1.199 (3)	N2—C6	1.366 (4)
O5—C18	1.246 (3)	N3—C14	1.452 (4)
O2—S1—O1	117.3 (1)	N3—S1—C13	103.9 (1)
O2—S1—N3	111.2 (1)	C12—N1—C11	110.5 (2)
O1—S1—N3	107.1 (1)	C12—N1—C10	113.4 (2)
O2—S1—C13	108.0 (1)	C11—N1—C10	111.4 (2)
O1—S1—C13	108.7 (1)	C7—N2—C6	109.4 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H2*A*···O5	0.88 (3)	1.84 (3)	2.710 (3)	168 (3)
N2—H1···O6^{i}	0.81 (3)	2.39 (3)	3.091 (3)	145 (3)
O3—H3*A*···O6^{ii}	0.90 (4)	1.66 (4)	2.519 (3)	159 (4)
N3—H3···O5^{iii}	0.80 (4)	2.03 (4)	2.811 (3)	164 (4)
C10—H10*B*···O1^{iv}	0.97	2.42	3.347 (3)	160
C12—H12*A*···O2^{v}	0.96	2.41	3.337 (4)	163
C13—H13*A*···O4^{ii}	0.97	2.39	3.337 (4)	164

Symmetry codes: (i) $1-x, 1-y, -z$; (ii) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iii) $-x, \frac{1}{2}+y, \frac{1}{2}-z$; (iv) $-x, 1-y, -z$; (v) $x, y-1, z$.

The H atoms attached to atoms N1, N2, N3 and O3 were located in difference electron density maps and were refined isotropically [N—

H = 0.80 (4)–0.89 (3) Å and O—H = 0.90 (4) Å]. The remaining H atoms were positioned geometrically and treated as riding on their parent C atoms, with C—H distances of 0.93–0.97 Å, and with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(C) for other H atoms. The methyl groups were allowed to rotate but not to tip.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT* (Bruker, 2001); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997) and *PLATON* (Spek, 2003); software used to prepare material for publication: *SHELXL*97 and *PARST* (Nardelli, 1995).

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