

## Doxylamine hydrogen succinate

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The crystal structure of doxylamine hydrogen succinate or dimethyl[[1-phenyl-1-(2-pyridyl)ethoxy]ethyl]ammonium hydrogen succinate,  $C_{17}H_{23}N_2O^+ \cdot C_4H_5O_4^-$ , contains two independent protonated molecules of doxylamine with different conformations and two succinate anions in an asymmetric unit. The structure is stabilized by hydrogen bonds involving the cations and the anions, with  $O \cdots O$  and  $N \cdots O$  distances in the range 2.536 (5)–2.853 (5) Å.

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## Key indicators

Single-crystal X-ray study

T = 293 K

Mean  $\sigma(C-C)$  = 0.009 Å

R factor = 0.067

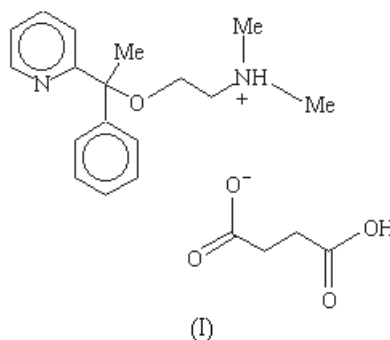
wR factor = 0.243

Data-to-parameter ratio = 19.3

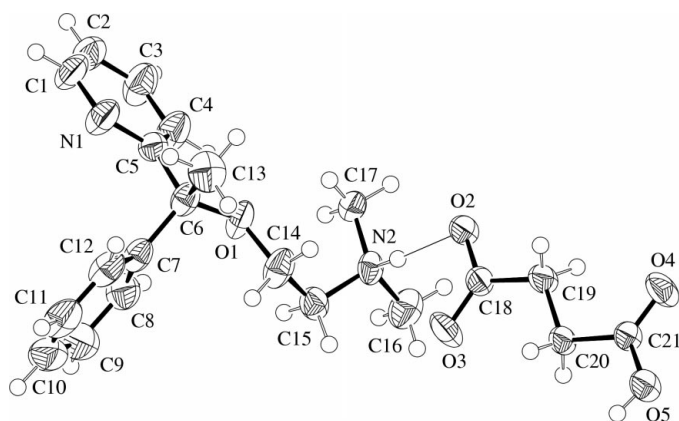
For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

## Comment

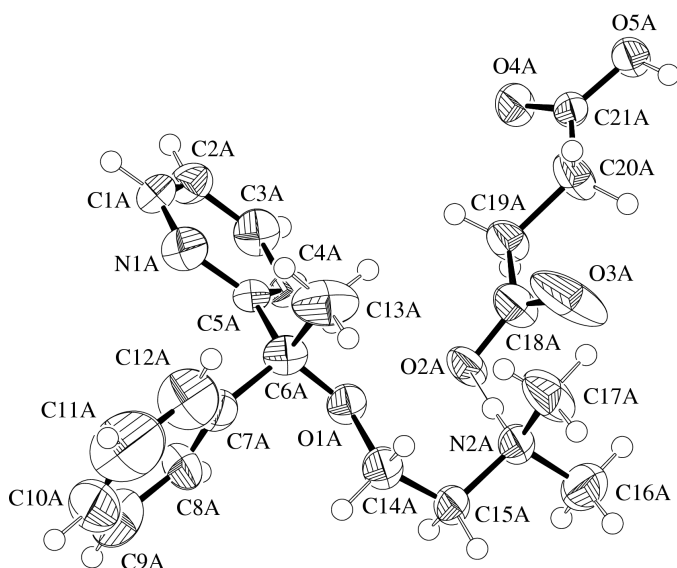
Doxylamine [dimethylaminoethoxy(methyl)benzylpyridine] is a chiral tertiary aminoalkyl ether, with antihistaminic actions on the  $H_1$ -receptor site (Casy, 1991). The crystal structures of the tetrachlorozincate(II), tetrachlorocobaltate(II) (Parvez & Sabir, 1998) and tetrachlorocuprate(II) (Braitenbach & Parvez, 2001) salts of doxylamine have been reported from our laboratory. The crystal structures of a number of compounds belonging to this class of ethers which possess antiallergic activities have been reported, *e.g.* diphenhydramine hydrochloride (Glaser & Maartmann-Moe, 1990), diphenhydramine thiourea complex (Wiedefeld & Knoch, 1987), carbinoxamine maleate (Bertolasi *et al.*, 1980) and clemastine hydrogen fumarate (Parvez & Wendling, 1991). The crystal structure of orphenadrine hydrochloride, a skeletal muscle relaxant, which is closely related to these compounds has also been reported (Glaser *et al.*, 1992). Continuing our investigations on the conformation of this important antiallergic drug, we now report the crystal structure of doxylamine hydrogen succinate, (I).



The asymmetric unit of (I) is composed of two cations of the antihistamine with different conformations and two hydrogen succinate ions (Fig. 1). The C9A–C12A atoms in one of the phenyl rings and the O3A atom had large displacement parameters possibly reflecting a degree of disorder.



**Figure 1**  
ORTEPII (Johnson, 1976) drawing of one of the two independent cation-anion pairs in (I). Displacement ellipsoids have been plotted at the 50% probability level.



**Figure 2**  
ORTEPII (Johnson, 1976) drawing of the second of the two independent cation-anion pairs in (I). Displacement ellipsoids have been plotted at the 50% probability level.

In both cations in (I), the pyridine rings are planar; they are inclined by 84.6 (2) and 85.9 (2)° to the phenyl rings. The corresponding angles in the tetrachlorozincate(II), tetrachlorocobaltate(II) (Parvez & Sabir, 1998) and tetrachlorocuprate(II) (Braitenbach & Parvez, 2001) salts of doxylamine were 87.68 (14), 88.1 (2) and 82.9 (3)°, respectively.

The orientations of the pyridyl rings in both cations in (I) are different from their conformations in the dihydrocations salts of doxylamine mentioned above, wherein both lone electron pairs of ethereal O atoms were oriented towards ammonium and pyridinium H atoms. This difference in orientation is due to a lack of interactions between ethereal O and pyridyl N atoms in (I) and results in a rotation of approximately 180° about the C5–C6 and C5A–C6A bonds in both cations of (I) as compared with those in the doxylamine moiety in the dihydro-cationic salts. Furthermore, the cations in (I) differ in the orientation of the aminomethyl

groups; the ammonium H atom of one of the cations has switched positions with a methyl group as compared to the other cation resulting in significantly different intramolecular separations between the ethereal O and ammonium N atoms: N2···O1 3.095 (6) versus N2A···O1A 2.870 (6) Å. The difference in the orientation of the aminomethyl groups in the two cations is evident from a comparison of the torsion angles O1–C14–C15–N2 76.9 (6)° and O1A–C14A–C15A–N2A 58.4 (6)°, and C14–C15–N2–C17 –62.0 (6)° and C14A–C15A–N2A–C17A 51.5 (6)°. The torsion angles corresponding to C5–C6–O1–C14, C6–O1–C14–C15 and C14–C15–N2–C17 in the two molecules are close to 180° with values in the range 173.2 (4)–179.5 (5)°, with the exception of C6–O1–C14–C15 of 155.7 (5)° in one of the cations.

In general, carboxylic acids tend to form cyclic dimers *via* hydrogen bonding. The crystal structure of (I) displays an extensive network of hydrogen bonding wherein the succinate ions are linked into chains in a zigzag fashion along the *c* axis, with O5···O2A and O5A···O2 being 2.538 (5) and 2.536 (5) Å, respectively. Only a few carboxylic acids appear to adopt this arrangement (Bernstein *et al.*, 1994), *e.g.* L-lysine succinate (Prasad & Vijayan, 1991). The cations are attached to the anion chains *via* ammonium H atoms involved in the N–H···O interactions with N2···O2 and N2A···O2A distances of 2.744 (5) and 2.853 (5) Å, respectively (see Table 1).

## Experimental

Crystals of (I) (Sigma Inc.) were grown from a solution in ethanol by slow evaporation at room temperature.

### Crystal data

$C_{17}H_{23}N_2O^+ \cdot C_4H_5O_4^-$   
 $M_r = 388.45$   
 Monoclinic,  $P2_1/c$   
 $a = 8.901$  (3) Å  
 $b = 21.075$  (4) Å  
 $c = 22.721$  (5) Å  
 $\beta = 97.22$  (2)°  
 $V = 4228.4$  (19) Å<sup>3</sup>  
 $Z = 8$

$D_x = 1.220$  Mg m<sup>-3</sup>  
 Mo  $K\alpha$  radiation  
 Cell parameters from 25 reflections  
 $\theta = 10.0$ – $15.0^\circ$   
 $\mu = 0.09$  mm<sup>-1</sup>  
 $T = 293$  (2) K  
 Prism, colourless  
 $0.40 \times 0.30 \times 0.30$  mm

### Data collection

Rigaku AFC-6S diffractometer  
 $\omega/2\theta$  scans  
 10 376 measured reflections  
 9763 independent reflections  
 2872 reflections with  $I > 2\sigma(I)$   
 $R_{int} = 0.06$   
 $\theta_{max} = 27.5^\circ$

$h = 0 \rightarrow 11$   
 $k = 0 \rightarrow 27$   
 $l = -29 \rightarrow 29$   
 3 standard reflections every 200 reflections  
 intensity decay: <0.1%

### Refinement

Refinement on  $F^2$   
 $R(F) = 0.067$   
 $wR(F^2) = 0.243$   
 $S = 1.04$   
 9763 reflections  
 507 parameters  
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0479P)^2 + 9.25P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{max} < 0.001$   
 $\Delta\rho_{max} = 0.42$  e Å<sup>-3</sup>  
 $\Delta\rho_{min} = -0.31$  e Å<sup>-3</sup>

**Table 1**

Hydrogen-bonding geometry (Å, °).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
N2—H1 $\cdots$ O2	0.91	1.85	2.744 (5)	166
N2A—H2 $\cdots$ O2A	0.91	2.01	2.853 (5)	153
O5—H3 $\cdots$ O2A <sup>i</sup>	0.82	1.73	2.538 (5)	171
O5A—H4 $\cdots$ O2 <sup>ii</sup>	0.82	1.72	2.536 (5)	171

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

All H atoms were located from difference maps and were included at geometrically idealized positions, with O—H = 0.82, N—H = 0.91 and C—H = 0.93–0.97 Å, in a riding mode with isotropic displacement parameters of 1.2 (non-methyl) and 1.5 (methyl) times the displacement parameters of the atoms to which they were attached.

Data collection: *MSC/AFSC Diffractometer Control Software* (Molecular Structure Corporation, 1988); cell refinement: *MSC/AFSC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1994); program(s) used to solve structure: *SAPI91* (Fan, 1991); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *TEXSAN*; software used to prepare material for publication: *SHELXL97* (Sheldrick, 1997).

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