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# Two succinic acid derivatives of 2-ethyl-6-methylpyridin-3-ol

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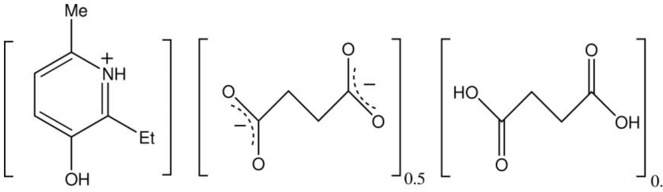
Crystals of bis(2-ethyl-3-hydroxy-6-methylpyridinium) succinate–succinic acid (1/1), $C_8H_{12}NO^+\cdot0.5C_4H_4O_4^{2-}\cdot0.5C_4H_6O_4$, (I), and 2-ethyl-3-hydroxy-6-methylpyridinium hydrogen succinate, $C_8H_{12}NO^+\cdot C_4H_5O_4^-$, (II), were obtained by reaction of 2-ethyl-6-methylpyridin-3-ol with succinic acid. The succinate anion and succinic acid molecule in (I) are located about centres of inversion. Intermolecular O—H⋯O, N—H⋯O and C—H⋯O hydrogen bonds are responsible for the formation of a three-dimensional network in the crystal structure of (I) and a two-dimensional network in the crystal structure of (II). Both structures are additionally stabilized by $\pi$–$\pi$ interactions between symmetry-related pyridine rings, forming a rod-like cationic arrangement for (I) and cationic dimers for (II).

## Comment

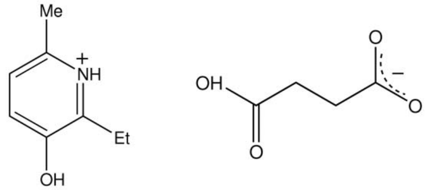
A succinic acid derivative of 2-ethyl-6-methylpyridin-3-ol is used as a nootropic drug in medical practice (Voronina, 1992, and references therein). It is also known for its antioxidant (Klebanov *et al.*, 2001), antihypoxant (Luk'yanova *et al.*, 1990), cardioprotective (Golikov *et al.*, 2004; Sidorenko *et al.*, 2011) and antistressor (Tilekeyeva & Sitina, 2005; Sariev & Kravtsova, 2005) effects. As no crystal data are available for any succinic acid derivatives of 2-ethyl-6-methylpyridin-3-ol [Cambridge Structural Database (CSD), Version 5.32, November 2010; Allen, 2002], in the present work we intended to obtain such structural information.

Our preliminary investigation, carried out by X-ray powder diffraction analysis, revealed that the reaction of 2-ethyl-6-methylpyridin-3-ol with succinic acid (1:1 molar ratio) could give either one crystalline compound or its mixture with another one (the ratio of these products depends on the reaction conditions). The aim of the present work was to obtain pure crystalline samples of the compounds and investigate their crystal structures using single-crystal X-ray diffraction.

One of the above-mentioned crystalline compounds, bis(2-ethyl-3-hydroxy-6-methylpyridinium) succinate–succinic acid (1/1), (I) (Fig. 1), was obtained directly as a result of the reaction of 2-ethyl-6-methylpyridin-3-ol with succinic acid. A pure sample of another compound, 2-ethyl-3-hydroxy-6-methylpyridinium hydrogen succinate, (II) (Fig. 2), can be prepared by transformation of (I) (see *Experimental*).



(I)



(II)

The asymmetric unit of (I) comprises one 2-ethyl-6-methyl-3-hydroxypyridinium cation, half a succinate anion (fully deprotonated) and half a succinic acid molecule. All atoms occupy general positions. The succinate anion and succinic acid molecule are located about centres of inversion, imposing $C_i$ symmetry on both components. However, their non-H-atom skeletons show almost planar configurations corresponding to noncrystallographic $C_{2h}$ symmetry, with r.m.s. deviations from planarity of 0.0056 Å for the succinic acid molecule and 0.0612 Å for the succinate anion (Pilati & Forni, 1998).

In (I), the bond lengths and valence angles are in the expected ranges for all components of the compound (CSD). In the carboxyl group of the succinic acid molecule, the C12—O121(H) bond length of 1.304 (2) Å is longer than the carbonyl-group C12—O122 bond length of 1.196 (2) Å. The C10—O101 and C10—O102 bond lengths of the carboxylate groups of the succinate anion are close to each other, being 1.2587 (18) and 1.2327 (19) Å, respectively.

There are hydrogen bonds in the crystal structure of (I) (Table 1 and Fig. 3). Intermolecular O—H⋯O hydrogen bonds between the succinic acid molecules and the succinate anions connect the components into polymeric chains extending along the [210] direction. Each 2-ethyl-3-hydroxy-6-methylpyridinium cation is bonded to three such polymeric chains through three hydrogen bonds, namely N—H⋯O, O—H⋯O and C—H⋯O, forming a three-dimensional polymeric network. There are additional $\pi$–$\pi$ interactions between the pyridine rings, with centroid–centroid ($Cg\cdots Cg$) distances of about 3.58 Å [$Cg\cdots Cg^{\rm v}$; symmetry code: (v) $-x, -y+1, -z+1$] and of about 3.74 Å [$Cg\cdots Cg^{\rm ii}$; symmetry code: (ii) $-x+1, -y+1, -z+1$]. These $\pi$–$\pi$ interactions result in the formation of a rod-like cationic arrangement extending along the *a* axis (Fig. 3).

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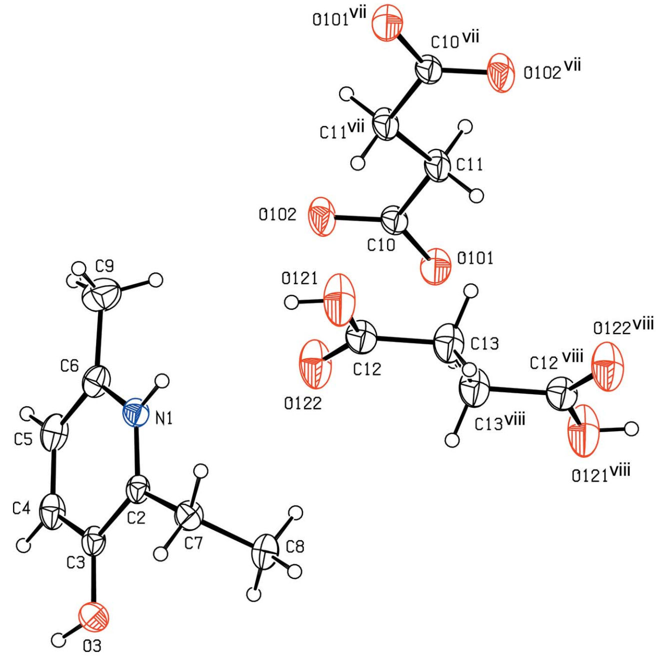

**Figure 1**
The molecular structure of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level. [Symmetry codes: (vii) $-x + 1, -y, -z$; (viii) $-x + 1, -y + 1, -z$.]

The asymmetric unit of (II) includes one 2-ethyl-3-hydroxy-6-methylpyridinium cation and one hydrogen succinate anion having only one deprotonated carboxyl group. All atoms lie on general positions. The non-H-atom skeleton of the hydrogen succinate anion is almost planar, with a mean deviation of the atoms from the least-squares plane of 0.0076 (12) Å. Bond lengths in the 2-ethyl-3-hydroxy-6-methylpyridinium cation and hydrogen succinate anion are similar to the corresponding values in (I).

The hydrogen bonds in the crystal structure of (II) (Table 2 and Fig. 4) are similar to those in (I), including intermolecular O—H···O, N—H···O and C—H···O hydrogen bonds. However, the supramolecular structure is somewhat different from that of (I). O—H···O hydrogen bonds between the succinate anions form infinite chains running along the *b* axis. Each 2-ethyl-3-hydroxy-6-methylpyridinium cation is connected to two anionic chains, to one *via* O—H···O and C—H···O hydrogen bonds and to the other through N—H···O

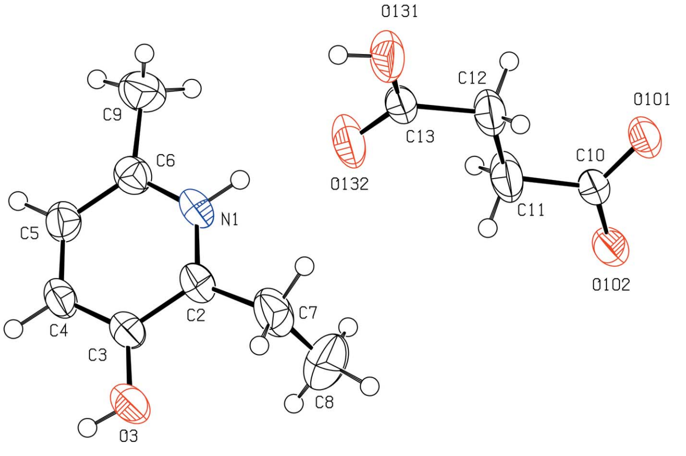

**Figure 2**
The asymmetric unit of (II), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 30% probability level.

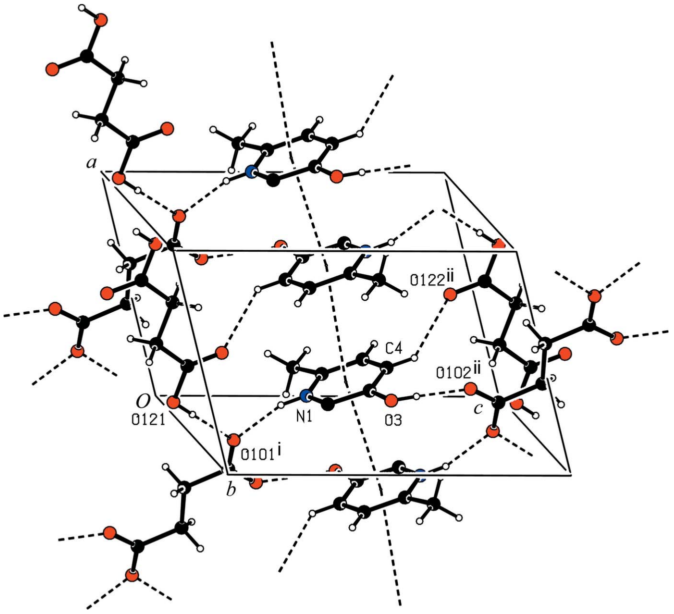

**Figure 3**
The hydrogen bonding (dashed lines) in the crystal structure of (I). Symmetry codes correspond to those in Table 1. $\pi$–$\pi$ interactions between the pyridine rings are also shown as dashed lines. The ethyl groups have been omitted for clarity.

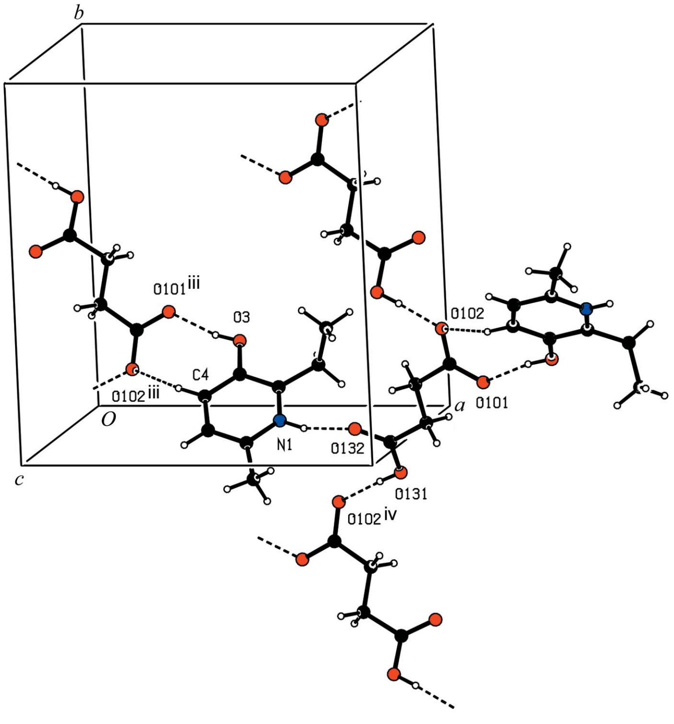

**Figure 4**
The hydrogen bonding (dashed lines) in the crystal structure of (II). Symmetry codes correspond to those in Table 2.

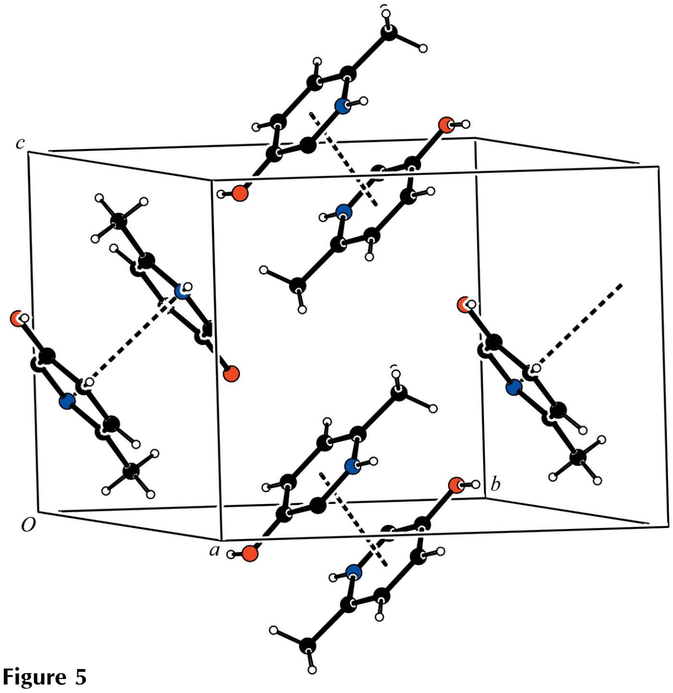

**Figure 5**
$\pi$–$\pi$ interactions (dashed lines) between the pyridine rings in the crystal structure of (II), forming cationic dimers. The ethyl groups of the cations and the succinate anions have been omitted for clarity.

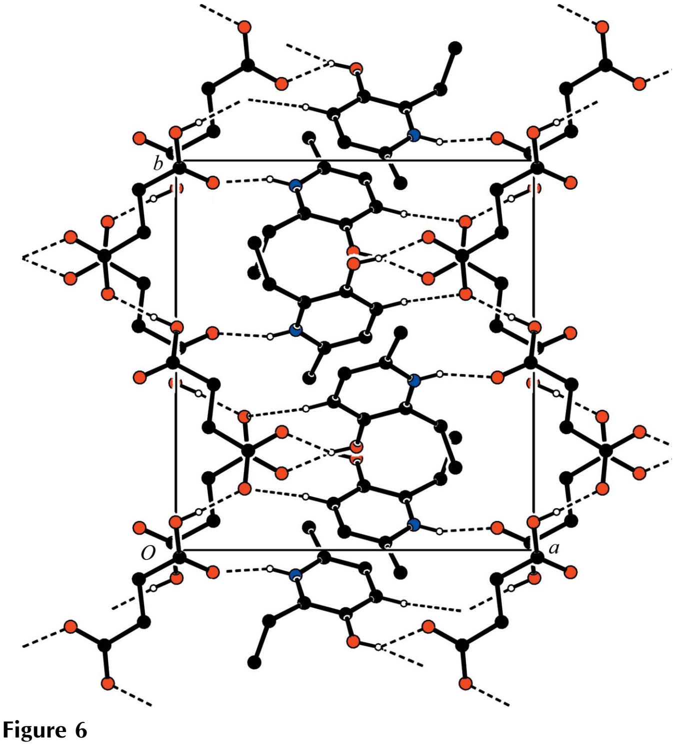

**Figure 6**
The crystal packing in (II), viewed along the *c* axis. Dashed lines show hydrogen bonds. Only H atoms participating in hydrogen bonds are shown.

hydrogen bonds, forming a two-dimensional network parallel to the $(10\overline{2})$ plane. There are also $\pi$–$\pi$ interactions between the pyridine rings, with centroid–centroid distances of about 3.52 Å [$Cg\cdots Cg^{vi}$; symmetry code: (vi) $-x + 1, -y, -z + 1$]. These are responsible for the formation of cationic dimers, shown in Fig. 5. The crystal packing of (II) is shown in Fig. 6.

## Experimental

For the synthesis of compound (I), 2-ethyl-6-methylpyridin-3-ol (10.0 g, 73 mmol) and succinic acid (8.6 g, 73 mmol) were heated in propan-2-ol under reflux for 1 h. The reaction mixture was filtered and the solution obtained was cooled to room temperature. The precipitated crystals of (I) were collected, washed twice with acetone (10 ml) and dried in air (yield 11.2 g, 44%; m.p. 385–386 K). $^1$H NMR (500 MHz, $D_2O$): $\delta$ 1.16 (*t*, 3H, *J* = 7.5 Hz, $CH_2CH_3$), 2.43 (*s*, 4H, $CH_2CH_2$), 2.48 (*s*, 3H, $CH_3$), 2.84 (*q*, 2H, *J* = 7.5 Hz, $CH_2CH_3$), 7.34 (*d*, 1H, *J* = 9 Hz, aryl), 7.66 (*d*, 1H, *J* = 9 Hz, aryl). Single crystals of (I) suitable for X-ray analysis were selected from the reaction product.

For the synthesis of (II), compound (I) (5.0 g) was dissolved in a propan-2-ol–acetone mixture (9:1 *v*/*v*, 70 ml) under reflux. After refluxing for 30 min, the solution obtained was cooled to room temperature. The precipitated crystals were collected and dried in air to give a mixture of (I) and (II), with a melting interval of 385–393 K. To prepare a pure sample of (II), the obtained mixture was heated at 388–391 K in an oil bath for 30 min. The resulting slurry was left to cool to room temperature overnight. The resulting crystalline solid of (II) was ground to a fine polycrystalline powder (yield 3.2 g, 64%; m.p. 392–393 K). The $^1$H NMR spectrum of (II) was identical to that of (I). Single crystals of (II) suitable for X-ray analysis can be prepared by crystallization from acetone solutions of (I) or (II), using seed crystals of (II). In the present work, a solution of (I) was used for this purpose.

## Compound (I)

### *Crystal data*

$C_8H_{12}NO^+\cdot 0.5C_4H_4O_4^{2-}\cdot 0.5C_4H_6O_4$
$M_r = 255.27$
Triclinic, $P\overline{1}$
$a = 7.3047\ (6)$ Å
$b = 8.4660\ (7)$ Å
$c = 11.7559\ (10)$ Å
$\alpha = 95.747\ (1)^\circ$
$\beta = 103.926\ (1)^\circ$
$\gamma = 107.716\ (1)^\circ$
$V = 660.25\ (10)$ Å$^3$
$Z = 2$
Mo $K\alpha$ radiation
$\mu = 0.10$ mm$^{-1}$
$T = 296$ K
0.40 × 0.20 × 0.15 mm

### *Data collection*

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2008)
$T_{min} = 0.961$, $T_{max} = 0.985$
6220 measured reflections
2717 independent reflections
2189 reflections with $I > 2\sigma(I)$
$R_{int} = 0.014$

### *Refinement*

$R[F^2 > 2\sigma(F^2)] = 0.045$
$wR(F^2) = 0.128$
$S = 1.03$
2717 reflections
167 parameters
H-atom parameters constrained
$\Delta\rho_{max} = 0.28$ e Å$^{-3}$
$\Delta\rho_{min} = -0.24$ e Å$^{-3}$

**Table 1**
Hydrogen-bond geometry (Å, °) for (I).

| $D$—H···$A$ | $D$—H | H···$A$ | $D$···$A$ | $D$—H···$A$ |
|---|---|---|---|---|
| N1—H1···O101$^i$ | 0.86 | 1.91 | 2.7367 (16) | 161 |
| O3—H3···O102$^{ii}$ | 0.82 | 1.74 | 2.5534 (15) | 176 |
| O121—H121···O101$^i$ | 0.82 | 1.78 | 2.6020 (18) | 180 |
| C4—H4···O122$^{ii}$ | 0.93 | 2.46 | 3.1719 (19) | 134 |

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

**Table 2**
Hydrogen-bond geometry (Å, °) for (II).

| $D$—H$\cdots$$A$ | $D$—H | H$\cdots$$A$ | $D$$\cdots$$A$ | $D$—H$\cdots$$A$ |
|---|---|---|---|---|
| N1—H1$\cdots$O132 | 0.86 | 1.92 | 2.7499 (17) | 161 |
| O3—H3$\cdots$O101$^{iii}$ | 0.82 | 1.75 | 2.5603 (15) | 167 |
| O131—H131$\cdots$O102$^{iv}$ | 0.82 | 1.67 | 2.4882 (16) | 177 |
| C4—H4$\cdots$O102$^{iii}$ | 0.93 | 2.53 | 3.3617 (19) | 149 |

Symmetry codes: (iii) $x - 1, -y + \frac{1}{2}, z - \frac{1}{2}$; (iv) $-x + 2, y - \frac{1}{2}, -z + \frac{3}{2}$.

### Compound (II)

*Crystal data*

$C_8H_{12}NO^+\cdot C_4H_5O_4^-$
$M_r$ = 255.27
Monoclinic, $P2_1/c$
$a$ = 11.4951 (2) Å
$b$ = 12.4787 (2) Å
$c$ = 9.1986 (1) Å
$\beta$ = 93.886 (1)°
$V$ = 1316.45 (3) Å$^3$
$Z$ = 4
Mo $K\alpha$ radiation
$\mu$ = 0.10 mm$^{-1}$
$T$ = 296 K
0.50 × 0.15 × 0.15 mm

*Data collection*

Bruker APEXII CCD area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Bruker, 2008)
$T_{min}$ = 0.952, $T_{max}$ = 0.985
12765 measured reflections
2733 independent reflections
2226 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.020

*Refinement*

$R[F^2 > 2\sigma(F^2)]$ = 0.047
$wR(F^2)$ = 0.141
$S$ = 1.03
2733 reflections
167 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.28 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.24 e Å$^{-3}$

H atoms were included in geometrically calculated positions, with N—H = 0.86 Å, O—H = 0.82 Å and C—H = 0.93 (aromatic), 0.96 (methyl) or 0.97 Å (methylene), and refined using a riding model, with $U_{iso}$(H) = 1.5$U_{eq}$(C,O) for methyl and hydroxy H atoms or 1.2$U_{eq}$(C,N) for other H atoms.

For both compounds, data collection: *APEX2* (Bruker, 2010); cell refinement: *SAINT* (Bruker, 2010); data reduction: *SAINT*; program(s) used to solve structure: *SIR2004* (Burla *et al.*, 2005); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: YF3010). Services for accessing these data are described at the back of the journal.

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