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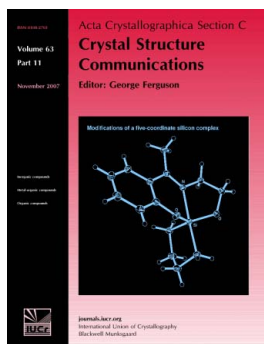
A new polymorph of succinylcholinium diiodide: comparison of succinylcholinium structures

Richard Pažout, Jaroslav Maixner, Michal Dušek and Bohumil Kratochvíl*Acta Cryst.* (2011). **C67**, o391–o393

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A new polymorph of succinylcholinium diiodide: comparison of succinylcholinium structures

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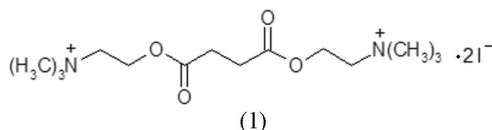
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The title compound {systematic name: trimethyl[2-({4-oxo-4-[2-(trimethylazaniumyl)ethoxy]butanoyl}oxy)ethyl]azanium diiodide}, $C_{14}H_{30}N_2O_4^{2+} \cdot 2I^-$, is a salt of the succinylcholinium cation. There is one formula unit in the asymmetric unit, represented by two anions and two halves of two cations which lie on centres of inversion. The component species are stabilized by electrostatic interactions, and C—H...I and C—H...O hydrogen bonds are also present.

Comment

Succinylcholine is used as a quaternary skeletal muscle relaxant. It is a paralytic drug used to induce muscle relaxation and short-term paralysis, usually to facilitate tracheal intubation (Thesleff, 1952). Succinylcholinium diiodide is used in surgical, anaesthetic and other procedures in which a brief period of muscle relaxation is called for.



Succinylcholinium diiodide, (1), exists in two polymorphic forms, as revealed by IR spectroscopy and X-ray powder diffraction. Polymorph I crystallizes in the space group $P2_1$ and its crystal structure was solved by Jensen (1970), who studied compounds acting as neuromuscular blocking agents. The newly prepared previously unknown polymorph II is the subject of this article (Fig. 1). Unlike polymorph I, polymorph II has a centrosymmetric crystal structure. The crystals are cube-like and colourless, while polymorph I forms elongated needles. Jensen (1970) pointed to ionic forces as the dominant feature in the structural packing.

The succinylcholinium cation consists of a 12-membered alkyl chain with no cyclic components. The central part of the chain

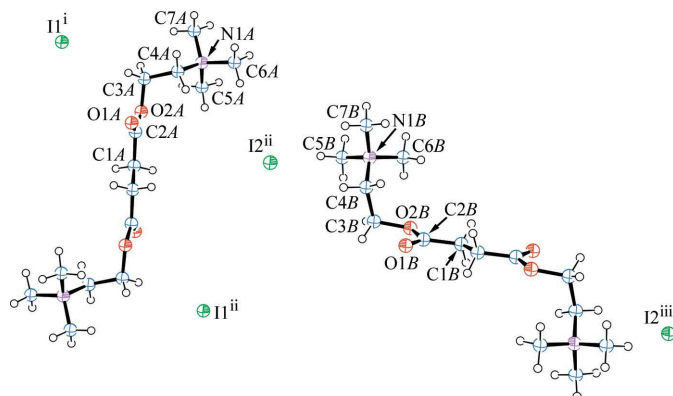


Figure 1

The molecular structure of polymorph II, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level. Unlabelled atoms are related to labelled atoms by the centre of inversion at $(-x + 1, -y + 1, -z + 2)$ for molecule *A* and at $(-x + 2, -y + 1, -z)$ for molecule *B*. [Symmetry codes: (i) $x, y, z + 1$; (ii) $-x + 1, -y + 1, -z + 1$; (iii) $x + 1, y, -z + 1$.]

is formed by the succinyl fragment and the peripheral parts by choline [or 2-(trimethylazaniumyl)ethyl]; together, they constitute the cationic part of the structure, with the iodide anions filling the voids between the chains.

The crystal structure of the title compound is built up of discrete moieties in the monoclinic space group $P2_1/c$, with one formula unit in the asymmetric unit comprising two anions and the halves of two symmetry-independent cations whose central C—C bonds lie across centres of inversion. The two half-cations in the asymmetric unit are nearly identical with respect to both their conformation and geometrical parameters.

The cations in polymorph II have an S-shaped conformation (Fig. 1). This is quite unlike the U-shape adopted by the cations of noncentrosymmetric polymorph I (Jensen, 1970). The S-shape can be converted into the U-form by two operations, each applied to either half of the cation: for example, in the case of cation *A*, one half of the cation is transformed by rotation around the C1A—C2A bond by approximately 180° , and the other half by reflection through the mirror plane approximately perpendicular to the C1Aⁱ—C1A—C2A plane [symmetry code: (i) $-x + 1, -y + 1, -z + 2$].

There is good agreement with regard to bond lengths. The C—C, C—O and C—N distances are very similar to those in polymorph I (Frydenvang & Jensen, 1996). The differences between the two polymorphs include the conformation of the H atoms on atoms C1 (both *A* and *B*) with respect to atom O1 of the carbonyl group, *viz.* essentially *cis* in polymorph I and *trans* in polymorph II. The C1ⁱ—C1—C2—O1 [symmetry code: (i) $-x + 1, -y + 1, -z + 2$ for cation *A*, $-x + 2, -y + 1, -z$ for cation *B*] torsion angles in polymorph II [$171.3(2)$ and $171.4(2)^\circ$, respectively] differ by 146 and 157° from the two independent corresponding torsion angles in polymorph I.

The conformational flexibility of the succinylcholinium moiety is shown by the variety of torsion angles of the cationic chain displayed by various succinylcholinium structures discussed below. The C2B—O2B—C3B—C4B and C2A—O2A—C3A—C4A torsion angles in polymorph II are $79.5(2)$

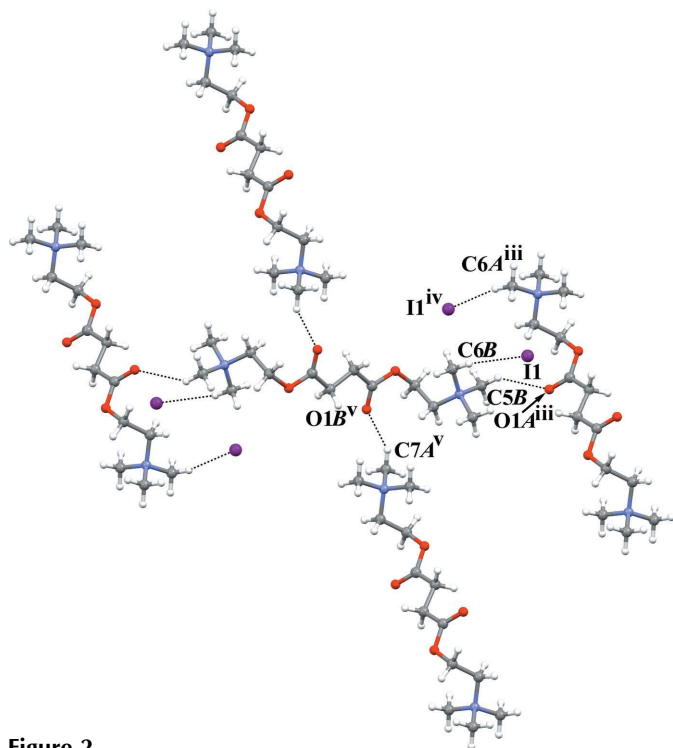


Figure 2

A view of the eight hydrogen bonds formed by two C—H···O and six long C—H···I interactions. Only H···I distances of less than 3.15 Å are considered. [Symmetry codes: (iii) $x, -y + \frac{3}{2}, z - \frac{1}{2}$; (iv) $-x + 1, y + \frac{1}{2}, -z + \frac{3}{2}$; (v) $x + 1, -y + \frac{3}{2}, z - \frac{1}{2}$]

and 79.9 (3)°, respectively, with the corresponding angles in polymorph I being 92.0 and 88.2°. The sections of the cation represented by O2B—C3B—C4B—N1B and O2A—C3A—C4A—N1A show even smaller differences, *viz.* 84.2 (2) and 87.8 (3)°, respectively, in polymorph II *versus* 80.2 and 79.4° in polymorph I.

The central chain between the C3 atoms (*i.e.* C3—O2—C2—C1—C1ⁱ—C2ⁱ—O2ⁱ—C3ⁱ) displays very similar torsion angles in the centrosymmetric structures of succinylcholinium cations. The difference appears when moving to the peripheral

part of the chain at the torsion angle C2—O2—C3—C4, showing that the flexibility occurs mainly at the O2—C3—C4 sequence and therefore the cholinium moiety in centrosymmetric structures may assume different conformations. All centrosymmetric succinylcholinium structures have the C2—O2—C3—C4 torsion angles between 159 and 175°, with the exception of the structure of polymorph II (this paper), where this torsion angle is 79.5 (2) and 79.9 (3)° for cations *A* and *B*, respectively. Another difference within the centrosymmetric structures is that some of them [Cambridge Structural Database (CSD; Allen, 2002) refcodes SUCPIC10 (Jensen, 1975) and VALVOU (Kazheva *et al.*, 2002)] have an approximately *cis* conformation of the H atoms on atom C1 with respect to carbonyl atom O1, while others [polymorph II (this paper), SUCCHO (Jensen, 1976), SUCHLO (Jensen, 1971) and VALVUA (Kazheva *et al.*, 2002)] assume a *trans* conformation. The structures with a *cis* conformation of this sequence have values for the C1ⁱ—C1—C2—O1 torsion angle of 159 (1)° (VALVOU) and 178.5° (SUCPI10), with this angle being between 5 and 10° in the *trans* structures.

A search of the CSD shows that all succinylcholinium structures which are centrosymmetric (in the space groups $P2_1/c$ or $P\bar{1}$) with the cation lying across a centre of inversion display an S-shape for the cation. There is one centrosymmetric structure in which the cation does not lie across a centre of inversion (VALVUA). It displays a pseudocentrosymmetric distorted S-shape with a central torsion angle of 163.9°, the structure being characteristic of an excess of iodide relative to the succinylcholinium moiety. The only known noncentrosymmetric succinylcholinium structure is that of polymorph I (SUCHOL01; Jensen, 1970).

Similarly to polymorph I, the structure of polymorph II is stabilized by electrostatic interactions, and ionic forces are the dominant feature (Frydenvang & Jensen, 1993). There are two systems of hydrogen-bond interactions, *viz.* C—H···O and C—H···I. While the former can be regarded as typical nonclassical hydrogen bonds, the long C—H···I interactions must be considered weak hydrogen bonds. If the H···I

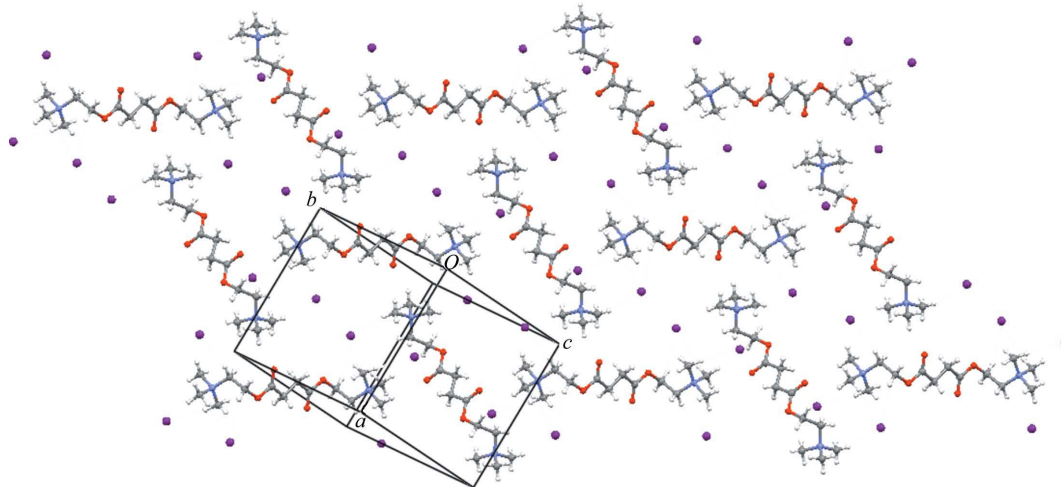


Figure 3

The chessboard packing of the succinylcholinium cations of polymorph II. Type *A* cations are inclined and type *B* cations are horizontal in this view.

distance is set to the sum of the relevant van der Waals radii (Bondi, 1964) plus 0.2 (3.38 Å), there are nine interactions on I1 and nine on I2, showing that the environment of both iodide ions is similar. If it is set to the sum of the van der Waals radii minus 0.12 (Jeffrey criterium; in this case 3.06 Å), only two interactions appear on I1 and none on I2.

The geometric parameters describing the C—H···I interactions in polymorph II are in accordance with the mean values of Desiraju & Steiner (1999). The observed values (average of 18 interactions within the H···I limit of 3.38 Å) are as follows: H···I = 3.2 Å compared with 3.16 (1) Å, C···I = 4.10 Å compared with 4.15 (1) Å and C—H···I angle = 152.9° compared with 152.8 (6)°.

For the purpose of clarity, Table 1 features only two C—H···I hydrogen bonds as defined by the Jeffrey criterium and two intermolecular C—H···O bonds: one strong with an H···A distance of 2.31 Å and the other weaker with a value of 2.50 Å. Similar contacts were described and summarized by Taylor & Kennard (1982).

There is much less in the literature regarding (ultra-)long C—H···I interactions. Similar H···I distances were observed in the structure of Dach Pt iodide, with distances between 2.97 and 3.10 Å (Pažout *et al.*, 2011). The same C—H···I interactions, with distances between 2.93 and 3.14 Å, are found in the structure of polymorph I, although Jensen (1970) did not consider them to be hydrogen bonds and mentioned C—I close contacts between 3.58 and 3.97 Å instead. Similar interactions were also reported by Frydenvang & Jensen (1996). The spatial arrangement of the cations shows horizontal *B* cations interspersed between inclined *A* cations (Fig. 3).

Experimental

The title compound was obtained as a gift from the pharmaceutical company Interpharma, Prague, Czech Republic. The crystals of polymorph (II) were crystallized from a hot solution in a 3:1 mixture of acetone and water, followed by cooling and isolation.

Crystal data

$C_{14}H_{30}N_2O_4^{2+} \cdot 2I^-$	$V = 2109.58 (8) \text{ \AA}^3$
$M_r = 544.2$	$Z = 4$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 11.6138 (2) \text{ \AA}$	$\mu = 3.00 \text{ mm}^{-1}$
$b = 13.0673 (3) \text{ \AA}$	$T = 151 \text{ K}$
$c = 13.9152 (3) \text{ \AA}$	$0.30 \times 0.28 \times 0.26 \text{ mm}$
$\beta = 92.6170 (15)^\circ$	

Data collection

Oxford Xcalibur Atlas Gemini	31136 measured reflections
Ultra diffractometer	5358 independent reflections
Absorption correction: multi-scan	4954 reflections with $I > 3\sigma(I)$
(<i>CrysAlis PRO</i> ; Oxford	$R_{\text{int}} = 0.018$
Diffracton, 2008)	
$T_{\text{min}} = 0.820$, $T_{\text{max}} = 1.000$	

Refinement

Refinement on F	199 parameters
$R[F^2 > 3\sigma(F^2)] = 0.019$	H-atom parameters constrained
$wR(F) = 0.038$	$\Delta\rho_{\text{max}} = 0.43 \text{ e \AA}^{-3}$
$S = 2.41$	$\Delta\rho_{\text{min}} = -0.33 \text{ e \AA}^{-3}$
5358 reflections	

Table 1

Hydrogen-bond geometry (Å, °).

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
$C6B-H3C6B \cdots I1$	0.96	3.04	3.984 (3)	168
$C6A-H1C6A \cdots I1^i$	0.96	3.05	3.991 (3)	167
$C7A-H2C7A \cdots O1B^{ii}$	0.96	2.31	3.176 (3)	150
$C5B-H2C5B \cdots O1A^{iii}$	0.96	2.50	3.184 (4)	128

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

A cube-like crystal was first measured on a diffractometer with Cu radiation, but even longer exposure times and the application of an analytical absorption correction did not result in data quality with an R_{int} value under 0.20. Therefore, the crystal was measured with Mo radiation, followed by a meticulous absorption correction consisting of refinement of the crystal shape accompanied by a multi-scan correction. The final R_{int} value was 0.018. All H atoms were first placed geometrically and then refined using a riding model, with C—H = 0.96 Å and $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$.

Data collection: *CrysAlis PRO* (Oxford Diffraction, 2008); cell refinement and data reduction: *CrysAlis RED* (Oxford Diffraction, 2008); structure solution: *SUPERFLIP* (Palatinus & Chapuis, 2007); program used to refine structure and prepare material for publication: *JANA2006* (Petříček *et al.*, 2006); molecular graphics: *ORTEP-3* (Farrugia, 1999) and *Mercury* (Version 2.3; Macrae *et al.*, 2008).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM3107). Services for accessing these data are described at the back of the journal.

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