organic compounds

4-(2-Carboxyethyl)morpholin-4-ium chloride

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The title compound, $C_7H_{14}NO_3^+ \cdot Cl^-$, is a hydrochloric acid salt of 3-(morpholin-4-yl)propionic acid, which is an important intermediate for the synthesis of biologically active heterocyclic compounds. The morpholine ring adopts a chair conformation with the hydrocarbon chain and the H atom on the N atom in equatorial and axial orientations, respectively. The structure is stabilized by a combination of strong $N-H \cdots Cl$ and $O-H \cdots Cl$ and weak $C-H \cdots O$ hydrogen bonds.

Related literature

For general background, see: Asselin & Humber (1977); Kelley *et al.* (1996); Meyer & Weintraub (1981); Boronnet *et al.* (1974).
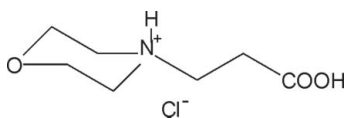
Experimental

Crystal data

C₇H₁₄NO₃⁺·Cl⁻
M_r = 195.64
Monoclinic, $P2_1/n$
a = 6.024 (2) Å
b = 11.593 (3) Å
c = 14.095 (6) Å
β = 97.72 (3)°

V = 975.4 (6) Å³
Z = 4
Mo $K\alpha$ radiation
μ = 0.36 mm⁻¹
T = 295 (2) K
0.36 × 0.30 × 0.10 mm

Data collection

Oxford Diffraction Xcalibur diffractometer
Absorption correction: none
2326 measured reflections
2244 independent reflections

1033 reflections with $I > 2\sigma(I)$
R_{int} = 0.034
3 standard reflections
  every 100 reflections
  intensity decay: none

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.133
S = 0.97
2244 reflections
115 parameters

H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.31 e Å⁻³
$\Delta\rho_{min}$ = −0.26 e Å⁻³

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

$D-H \cdots A$	$D-H$	$H \cdots A$	$D \cdots A$	$D-H \cdots A$
N1—H1N···Cl	0.91 (3)	2.18 (3)	3.092 (3)	176 (3)
O1—H1O···Clⁱ	0.99 (4)	2.04 (4)	3.008 (3)	164 (4)
C6—H6A···O2ⁱⁱ	0.97	2.65	3.491 (3)	145
C7—H7A···O2ⁱⁱ	0.97	2.40	3.337 (3)	162
C3—H3A···O4ⁱⁱⁱ	0.97	2.45	3.241 (4)	138
C3—H3B···O1ⁱᵛ	0.97	2.69	3.575 (3)	152
C7—H7B···O2ᵛ	0.97	2.69	3.445 (3)	136

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

Data collection: *CrysAlis CCD* (Oxford Diffraction, 2005); cell refinement: *CrysAlis RED* (Oxford Diffraction, 2005); data reduction: *CrysAlis RED*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL/PC* (Sheldrick, 1990); software used to prepare material for publication: *SHELXL97* and *enCIFer* (Allen *et al.*, 2004).

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: OM2177).

References

Allen, F. H., Johnson, O., Shields, G. P., Smith, B. R. & Towler, M. (2004). *J. Appl. Cryst.* **37**, 335–338.
Asselin, A. A. & Humber, L. G. (1977). US Patent 4 044 131.
Boronnet, R., Foussard, B. O., Bretaudeau, J. & Hubert, F. (1974). *Eur. J. Med. Chem.* **9**, 182–187.
Kelley, J. L., Musso, D. L., Boswell, G. E., Soroko, F. E. & Cooper, B. R. (1996). *J. Med. Chem.* **39**, 347–349.
Meyer, D. R. & Weintraub, P. M. (1981). *J. Heterocycl. Chem.* **18**, 451–453.
Oxford Diffraction (2005). *CrysAlis CCD* (Version 1.171) and *CrysAlis RED* (Version 1.171). Oxford Diffraction Ltd, Abingdon, Oxfordshire, England.
Sheldrick, G. M. (1990). *SHELXTL/PC*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.

supplementary materials

4-(2-Carboxyethyl)morpholin-4-ium chloride

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Comment

Morpholine derivatives are known to exhibit a wide spectrum of biological activities, including antifungal (Asselin & Humber, 1977), antidepressant (Kelley *et al.*, 1996) or anorectic (Meyer & Weintraub, 1981) properties. Additionally, they are used as an intermediate for the synthesis of the antispasmodic drugs and other biologically active heterocycles (Boronnet *et al.*, 1974). In view of the versatility of these compounds, the title compound was synthesized and we herein report its molecular and crystal structure.

In the crystal structure of the proton is transferred from the hydrochloride molecule to the morpholine N1 atom, as confirmed by location of the H atom in a difference Fourier map, leading to coexistence of the hydrogen-bonded 3-morpholin-4-yl-propionic cation and chloride anion. The morpholine ring adopts the usual chair conformation with the C7 atom at the equatorial and the H1N proton at the axial position. The hydrocarbon $(CH_2)_2COOH$ chain exists in the extended *trans* conformation, which is reflected in the values of the N1—C7—C8—C9 and C7—C8—C9—O1 torsion angles of −168.0 (3) and 178.5 (3)°, respectively. The carboxyl group has the typical *cis* conformation with the O2—C9—O1—H1O torsion angle of 6.0 (4)°. The dihedral angle between the best plane of the hydrocarbon chain and C2/C3/C5/C6 ring atoms is 36.9 (4)°. The bond distances and angles are within the expected ranges observed for related compounds.

The strong N3—H3o⋯Cl hydrogen bonds (Table 1) are observed between ionic pairs. The Cl⁻ ion forms also H-bond with the carboxylic O1—H1O proton from the adjacent cation. As can be seen in Fig. 2, one-dimensional cationic chains, propagated along the [101] direction, can be distinguished in the structure. Within the chain the cations lacated around the (0, 1/2, 1/2) inversion centre are connected together through chelating C6—H6A⋯O2[ii] and C7—H7A⋯O2[ii] hydrogen bonds. The C3—H3A⋯O4[iii] H-bonds links cations located around the next (1/2, 1, 1) center of symmetry. The cationic layers are associated into three-dimensional structure primarily by interactions involving the chloride anions.

Experimental

A mixture of 3-morpholin-4-yl-propionic acid hydrazide (0.01 mol) and 4,4'-methylene-bis(phenylisocyanate) (0.01 mol) was heated at the temperature 383–393 K for 20 h. The product, 4,4'-methylene-bis{[1-(3-morpholin-4-yl-propionic)-4-phenyl]semicarbazide} was washed with diethyl ether to remove the unreacted isocyanate, dried and crystallized from ethanol (yield 83%). The final product, 3-morpholin-4-yl-propionic acid hydrochloride, was prepared by refluxing semicarbazide with 2% NaOH (40 ml) for 15 h. After cooling, the solution was neutralized with dilute hydrochloric acid. The product was filtered and recrystallized from ethanol (m.p. 353–356 K, yield 89%). Anal. Calcd. for $C_7H_{14}NO_3Cl$: C, 42.96; H, 7.21; N, 7.15%; found: C, 42.91; H, 7.30; N, 7.18%. ^{1}H NMR (300 MHz, DMSO-d_6, p.p.m.): δ 2.87 (2*H*, t, CH_2); 2.98–3.06 (4*H*, m, 2CH_2); 3.27 (2*H*, t, CH_2); 3.77–3.87 (4*H*, m, 2CH_2); 11.98 (1*H*, s, OH).

supplementary materials

Refinement

H atoms bonded to O1 and N1 atoms were located in the difference Fourier map and refined. Other H atoms were positioned geometrically and allowed to ride on their parent atoms, with C—H bond distances of 0.97 Å. The displacement parameters of the H atoms were $U_{iso}(H) = 1.2\ U_{eq}(C)$.
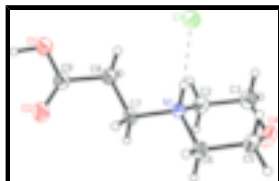
Figures

Fig. 1. The molecular structure showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level. N—H···Cl hydrogen bond is shown as dashed line.
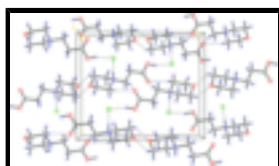

Fig. 2. The molecular packing viewed down the a axis. Dashed lines indicate hydrogen bonds.

4-(2-Carboxyethyl)morpholin-4-ium chloride

Crystal data

$C_7H_{14}NO_3{}^+ \cdot Cl^-$	$F_{000} = 416$
$M_r = 195.64$	$D_x = 1.332$ Mg m^{-3}
Monoclinic, $P2_1/n$	Mo $K\alpha$ radiation $\lambda = 0.71073$ Å
Hall symbol: -P 2yn	Cell parameters from 62 reflections
$a = 6.024\ (2)$ Å	$\theta = 5–12º$
$b = 11.593\ (3)$ Å	$\mu = 0.36$ mm^{-1}
$c = 14.095\ (6)$ Å	$T = 295\ (2)$ K
$\beta = 97.72\ (3)º$	Plate, colourless
$V = 975.4\ (6)$ Å^3	$0.36 \times 0.30 \times 0.10$ mm
$Z = 4$	

Data collection

Oxford Diffraction Xcalibur diffractometer	$R_{int} = 0.034$
Radiation source: fine-focus sealed tube	$\theta_{max} = 27.6º$
Monochromator: graphite	$\theta_{min} = 2.3º$
$T = 295(2)$ K	$h = -7 \rightarrow 7$
$\omega/2\theta$ scans	$k = 0 \rightarrow 15$
Absorption correction: none	$l = -18 \rightarrow 0$
2326 measured reflections	3 standard reflections

2244 independent reflections

1033 reflections with $I > 2\sigma(I)$

every 100 reflections

intensity decay: 0.03%

Refinement

Refinement on F^2	Secondary atom site location: difference Fourier map
Least-squares matrix: full	Hydrogen site location: inferred from neighbouring sites
$R[F^2 > 2\sigma(F^2)] = 0.054$	H atoms treated by a mixture of independent and constrained refinement
$wR(F^2) = 0.133$	$w = 1/[\sigma^2(F_o^2) + (0.0671P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.97$	$(\Delta/\sigma)_{max} < 0.001$
2244 reflections	$\Delta\rho_{max} = 0.31$ e Å^{-3}
115 parameters	$\Delta\rho_{min} = -0.26$ e Å^{-3}
Primary atom site location: structure-invariant direct methods	Extinction correction: none

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R-factor wR and goodness of fit S are based on F^2, conventional R-factors R are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2sigma(F^2)$ is used only for calculating R-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R– factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	y	z	$U_{iso}*/U_{eq}$
Cl	−0.11080 (14)	0.77228 (7)	0.73370 (6)	0.0430 (2)
O1	0.3892 (5)	0.7281 (2)	0.44710 (19)	0.0718 (8)
H1O	0.401 (7)	0.713 (4)	0.379 (3)	0.086*
O2	0.2681 (4)	0.5478 (2)	0.44468 (16)	0.0580 (7)
C9	0.3233 (5)	0.6344 (3)	0.4881 (2)	0.0415 (8)
C8	0.3297 (6)	0.6491 (3)	0.5935 (2)	0.0448 (8)
H8A	0.2363	0.7140	0.6061	0.054*
H8B	0.4819	0.6656	0.6221	0.054*
C7	0.2479 (6)	0.5419 (2)	0.6384 (2)	0.0406 (7)
H7A	0.1101	0.5161	0.6008	0.049*
H7B	0.3584	0.4812	0.6374	0.049*
N1	0.2066 (4)	0.5621 (2)	0.73937 (16)	0.0315 (5)
H1N	0.114 (5)	0.624 (3)	0.741 (2)	0.038*
C2	0.4146 (5)	0.5824 (3)	0.8066 (2)	0.0434 (8)
H2A	0.4905	0.6504	0.7869	0.052*

H2B	0.5145	0.5170	0.8052	0.052*
C3	0.3592 (6)	0.5992 (3)	0.9067 (2)	0.0511 (8)
H3A	0.4962	0.6115	0.9501	0.061*
H3B	0.2658	0.6671	0.9086	0.061*
O4	0.2450 (4)	0.5014 (2)	0.93676 (16)	0.0550 (7)
C5	0.0404 (6)	0.4839 (3)	0.8757 (2)	0.0459 (8)
H5A	−0.0541	0.5514	0.8779	0.055*
H5B	−0.0376	0.4184	0.8985	0.055*
C6	0.0796 (5)	0.4627 (2)	0.7742 (2)	0.0397 (7)
H6A	−0.0629	0.4539	0.7338	0.048*
H6B	0.1644	0.3920	0.7708	0.048*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl	0.0448 (4)	0.0416 (4)	0.0444 (4)	−0.0075 (4)	0.0131 (3)	0.0005 (4)
O1	0.124 (2)	0.0516 (13)	0.0467 (14)	−0.0211 (16)	0.0360 (16)	−0.0001 (13)
O2	0.0743 (18)	0.0602 (15)	0.0420 (13)	−0.0196 (13)	0.0168 (12)	−0.0035 (11)
C9	0.0377 (17)	0.0478 (18)	0.0415 (19)	−0.0011 (15)	0.0153 (15)	0.0029 (15)
C8	0.054 (2)	0.0422 (16)	0.0411 (19)	−0.0106 (16)	0.0171 (16)	−0.0017 (15)
C7	0.0509 (19)	0.0402 (16)	0.0341 (16)	−0.0062 (15)	0.0181 (15)	−0.0051 (13)
N1	0.0318 (14)	0.0330 (12)	0.0311 (13)	0.0003 (11)	0.0090 (11)	0.0004 (10)
C2	0.0343 (17)	0.0495 (18)	0.0464 (19)	−0.0020 (14)	0.0054 (14)	0.0033 (15)
C3	0.048 (2)	0.061 (2)	0.0410 (19)	−0.0043 (17)	−0.0039 (16)	0.0017 (17)
O4	0.0500 (14)	0.0733 (16)	0.0410 (14)	−0.0037 (13)	0.0037 (11)	0.0169 (11)
C5	0.0445 (19)	0.055 (2)	0.0409 (18)	−0.0036 (16)	0.0146 (16)	0.0072 (15)
C6	0.0399 (19)	0.0384 (16)	0.0430 (18)	−0.0038 (13)	0.0132 (15)	0.0038 (14)

Geometric parameters (Å, °)

O1—C9	1.316 (4)	C2—C3	1.505 (5)
O1—H1o	0.99 (4)	C2—H2A	0.9700
O2—C9	1.200 (4)	C2—H2B	0.9700
C9—C8	1.492 (4)	C3—O4	1.420 (4)
C8—C7	1.506 (4)	C3—H3A	0.9700
C8—H8A	0.9700	C3—H3B	0.9700
C8—H8B	0.9700	O4—C5	1.420 (4)
C7—N1	1.496 (4)	C5—C6	1.502 (4)
C7—H7A	0.9700	C5—H5A	0.9700
C7—H7B	0.9700	C5—H5B	0.9700
N1—C2	1.485 (4)	C6—H6A	0.9700
N1—C6	1.502 (3)	C6—H6B	0.9700
N1—H1N	0.91 (3)		
C9—O1—H1o	111 (2)	C3—C2—H2A	109.6
O2—C9—O1	123.1 (3)	N1—C2—H2B	109.6
O2—C9—C8	124.9 (3)	C3—C2—H2B	109.6
O1—C9—C8	112.0 (3)	H2A—C2—H2B	108.1
C9—C8—C7	111.0 (3)	O4—C3—C2	110.7 (3)

C9—C8—H8A	109.4	O4—C3—H3A	109.5
C7—C8—H8A	109.4	C2—C3—H3A	109.5
C9—C8—H8B	109.4	O4—C3—H3B	109.5
C7—C8—H8B	109.4	C2—C3—H3B	109.5
H8A—C8—H8B	108.0	H3A—C3—H3B	108.1
N1—C7—C8	112.1 (2)	C3—O4—C5	110.4 (2)
N1—C7—H7A	109.2	O4—C5—C6	111.5 (3)
C8—C7—H7A	109.2	O4—C5—H5A	109.3
N1—C7—H7B	109.2	C6—C5—H5A	109.3
C8—C7—H7B	109.2	O4—C5—H5B	109.3
H7A—C7—H7B	107.9	C6—C5—H5B	109.3
C2—N1—C7	113.5 (2)	H5A—C5—H5B	108.0
C2—N1—C6	109.7 (2)	C5—C6—N1	109.7 (2)
C7—N1—C6	110.4 (2)	C5—C6—H6A	109.7
C2—N1—H1N	109.0 (19)	N1—C6—H6A	109.7
C7—N1—H1N	108.9 (18)	C5—C6—H6B	109.7
C6—N1—H1N	105.2 (19)	N1—C6—H6B	109.7
N1—C2—C3	110.1 (3)	H6A—C6—H6B	108.2
N1—C2—H2A	109.6		
O2—C9—C8—C7	−2.4 (5)	N1—C2—C3—O4	58.5 (3)
O1—C9—C8—C7	178.5 (3)	C2—C3—O4—C5	−60.9 (3)
C9—C8—C7—N1	−168.0 (3)	C3—O4—C5—C6	60.8 (3)
C8—C7—N1—C2	−68.7 (3)	O4—C5—C6—N1	−57.3 (3)
C8—C7—N1—C6	167.7 (3)	C2—N1—C6—C5	54.0 (3)
C7—N1—C2—C3	−178.7 (3)	C7—N1—C6—C5	179.8 (3)
C6—N1—C2—C3	−54.8 (3)		

Hydrogen-bond geometry (Å, °)

D—H⋯A	D—H	H⋯A	D⋯A	D—H⋯A
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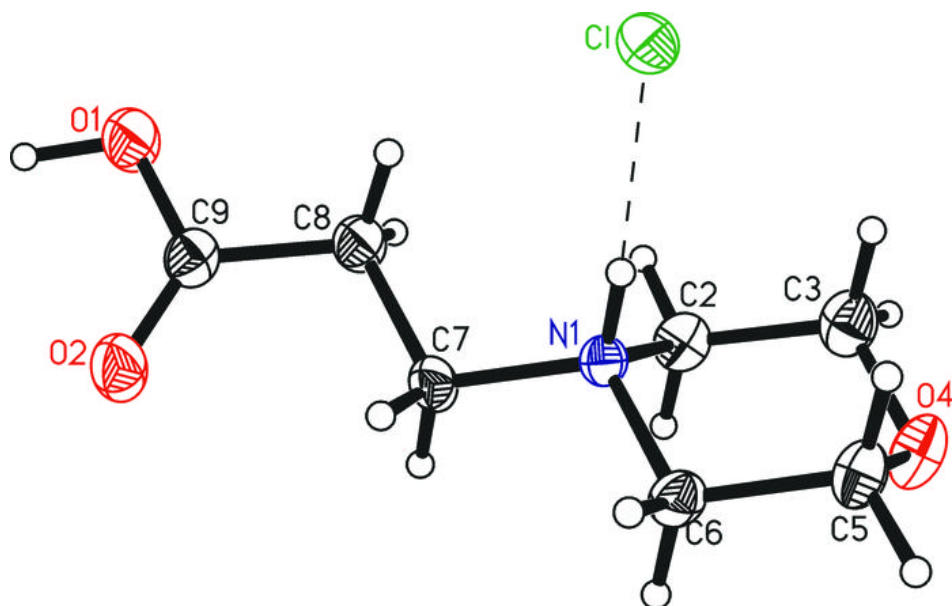
Fig. 1

Fig. 2