Acta Cryst. (1997). C**53**, 1677–1679

2-(4-Chlorophenyl)-2-(*N*-acetylcarbamoylthio)ethanoic Acid–Acetonitrile (1/1)

IVAN LEBAN,[a] ALENKA MAJCEN LE MARÉCHAL[b] AND ALBERT ROBERT[c]

[a]*Faculty of Chemistry and Chemical Technology, University of Ljubljana, Aškerčeva 5, PO Box 537, SI-1001 Ljubljana, Slovenia,* [b]*Faculty of Mechanical Engineering, University of Maribor, Smetanova 17, SI-2000 Maribor, Slovenia, and* [c]*Laboratoire de Synthese et Electrosynthese Organique, UMR 6510, Université de Rennes I, Avenue du Général Leclerc, F-35042 Rennes Cédex, France. E-mail: ivan.leban@uni-lj.si*

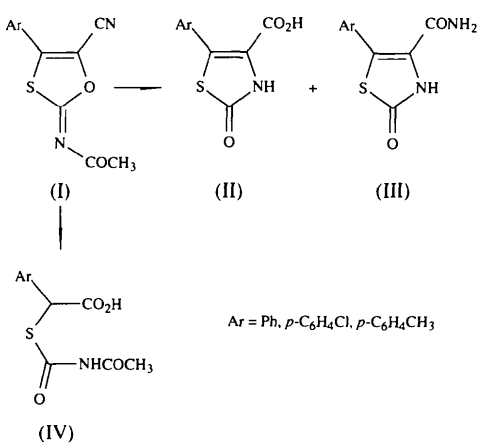
(*Received 11 April 1997; accepted 10 June 1997*)

Abstract

The hydrolysis of 2-acetylimino-4-(4-chlorophenyl)-1,3-oxathiole-5-carbonitrile in air results in 2-(4-chlorophenyl)-2-(*N*-acetylcarbamoylthio)ethanoic acid, which forms a 1:1 adduct with a solvent acetonitrile molecule, $C_{11}H_{10}ClNO_4S.C_2H_3N$. Even after ring opening there still exists a short intramolecular S···O interaction [2.660 (3) Å]. The bond lengths are normal and in agreement with expected values.

Comment

Substituted 1,3-oxathioles, (I), obtained from *gem*-dicyano epoxides can be hydrolysed in concentrated hydrochloric acid to give either (II) or (III) or a mixture (Majcen Le Maréchal, Robert & Leban, 1993). Although relatively stable, compounds of type (I) transform slowly in the presence of the air at room temperature to type (IV). The structure of the 2-(4-chlorophenyl)-2-(*N*-acetylthiocarbamato)ethanoic acid–acetonitrile (1/1) adduct, (IV).CH_3CN (Ar = *p*-C_6H_4Cl), has been determined and is presented here.



The molecule with the same atomic numbering scheme as used by Majcen Le Maréchal, Robert & Leban (1993) is depicted in Fig. 1. Selected bond distances, angles and torsion angles are given in Table 1.

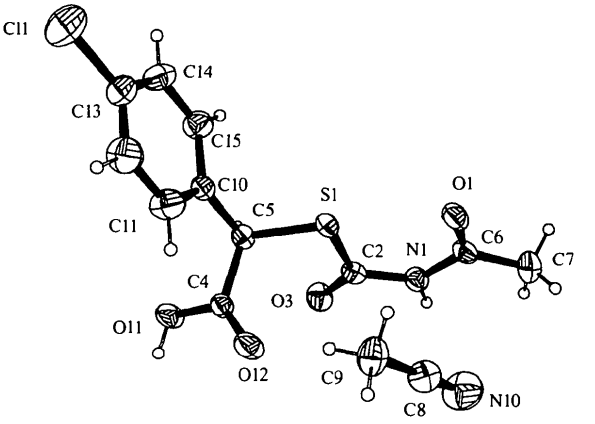


Fig. 1. *ORTEP*II (Johnson, 1971) view of the title adduct with the atomic numbering. Anisotropic displacement ellipsoids are drawn at the 30% probability level. H atoms are of arbitrary size.

The bond lengths are normal and in agreement with expected values. The most interesting feature of the structure is the nearly planar arrangement of the atoms S1, C2, N1, C6 and O1 [to within 0.014 (2) Å]; an S1···O1 interaction of 2.660 (3) Å has a C5—S1···O1 angle of 172.8 (1)°. These values fit well with the distribution of directional preferences for substituents (Rosenfield, Parthasarathy & Dunitz, 1977). The above examination showed that electrophiles tend to approach the divalent S atom at roughly 20° from the perpendicular to the plane through atoms *Y*—S—*Z*, while nucleophiles (this case) tend to approach approximately along the extension of one of the covalent bonds, either *Y*—S or *Z*—S. There is a suggestion that the LUMO (lowest unoccupied molecular orbital) σ^*(S—*Y*) or σ^*(S—*Z*) orbitals are involved in this type of interaction. Our results are also in agreement with the survey of *X*—S···O=*Y* interactions by Kálmán & Párkányi (1980). A similar S···O value of 2.579 (7) Å was also found in the precursor of this compound, (I) (Majcen Le Maréchal, Robert & Leban, 1993). The same planar pentacyclic arrangement with S···O interaction was found in a search of the Cambridge Structural Database (Allen, Kennard & Taylor, 1983) for more than 70 compounds. The basic motif of these structures is the divalent S atom mostly in a five-membered heterocyclic ring (*e.g.* oxathiole) with the neighbouring three atoms, N—C=O, forming together with the S···O interaction another five-membered ring.

The phenyl-ring plane, (*a*) (C10–C15), the carboxylic group plane, (*b*) (O11, O12, C4, C5), and the plane of S1, C2, N1, C6 and O1, (*c*), are planar to

within 0.007 (3), 0.009 (3) and 0.014 (2) Å, respectively. The corresponding dihedral angles are: (*a*)/(*b*) 85.7 (1), (*b*)/(*c*) 74.3 (1) and (*a*)/(*c*) 83.0 (1)°.

The molecules of the title compound are linked together by a hydrogen bond between the carboxylic group C4—O11—H and the carbonyl O atom, O1, of a neighbouring molecule. One molecule of the acetonitrile solvent (CH_3CN) is bonded by a weak hydrogen bond of the type N···H—N to the nitrogen of the acetylcarbamoylthio group (details are given in Table 2).

Table 1. *Selected geometric parameters (Å, °)*

S1—C2	1.765 (3)	N1—C6	1.368 (4)
S1—C5	1.820 (3)	C6—O1	1.223 (4)
C2—O3	1.204 (3)	C6—C7	1.503 (5)
C2—N1	1.389 (4)	C13—C11	1.733 (4)
C4—O12	1.188 (4)	C9—C8	1.443 (5)
C4—O11	1.308 (4)	C8—N10	1.128 (5)
C4—C5	1.515 (4)		
C2—S1—C5	96.06 (15)	C4—C5—S1	111.9 (2)
O3—C2—N1	119.4 (3)	C10—C5—S1	108.0 (2)
O3—C2—S1	122.9 (3)	C6—N1—C2	127.1 (3)
N1—C2—S1	117.6 (2)	O1—C6—N1	121.0 (3)
O12—C4—O11	123.7 (3)	O1—C6—C7	123.0 (3)
O12—C4—C5	125.4 (3)	N1—C6—C7	116.0 (3)
O11—C4—C5	110.8 (3)	N10—C8—C9	179.5 (4)
C4—C5—C10	112.4 (3)		
C5—S1—C2—O3	0.4 (3)	O3—C2—N1—C6	177.3 (3)
C5—S1—C2—N1	−179.1 (2)	S1—C2—N1—C6	−3.2 (4)
C2—S1—C5—C4	66.5 (2)	C2—N1—C6—O1	2.3 (5)
C2—S1—C5—C10	−169.3 (2)	C2—N1—C6—C7	−179.4 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O11—H2···O1^{i}	0.820	1.851	2.654 (3)	166
N1—H3···N10^{ii}	0.860	2.096	2.953 (5)	174

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

Experimental

Compound (I) was prepared from the appropriate epoxide and KSCN in acetic anhydride Ac_2O solution. After 3 h, the reaction mixture was cooled in the refrigerator for 30 min; (I) was filtered off, washed with water and recrystallized from ethanol (Majcen Le Maréchal, Robert & Leban, 1993). In air, (I) slowly transformed to an oil, which was dissolved in acetonitrile. Single crystals of (IV).CH_3CN (Ar = *p*-C_6H_4Cl) were obtained on slow evaporation and sealed in glass capillaries.

Crystal data

$C_{11}H_{10}ClNO_4S.C_2H_3N$
M_r = 328.76
Orthorhombic
Pbca
a = 34.050 (5) Å
b = 11.300 (3) Å
c = 8.347 (2) Å
V = 3211.6 (12) Å^3
Z = 8
D_x = 1.360 Mg m^{-3}
D_m = 1.35 (5) Mg m^{-3}
D_m measured by flotation
Mo $K\alpha$ radiation
λ = 0.71073 Å
Cell parameters from 25 reflections
θ = 10–12°
μ = 0.383 mm^{-1}
T = 293 (2) K
Plate
0.34 × 0.29 × 0.23 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
Variable $\theta/2\theta$ scans
Absorption correction: none
5407 measured reflections
2820 independent reflections
1734 reflections with $I > 2\sigma(I)$
R_{int} = 0.049
θ_{max} = 25.0°
$h = 0 \rightarrow 40$
$k = 0 \rightarrow 13$
$l = 0 \rightarrow 9$
3 standard reflections every 150 reflections
intensity decay: 13.7%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.122
S = 1.038
2815 reflections
190 parameters
H atoms not refined
$w = 1/[\sigma^2(F_o^2) + (0.0402P)^2 + 1.6415P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.067
$\Delta\rho_{max}$ = 0.220 e Å^{-3}
$\Delta\rho_{min}$ = −0.264 e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for Crystallography* (Vol. C)

The space group *Pbca* was deduced from the systematic absences. All H atoms were found in the difference electron-density map and were included in the refinement at calculated positions with isotropic displacement parameters taken from the attached heavy atoms and multiplied by 1.3 (or 1.6 for methyl H atoms). The prepared crystals exhibited considerable decomposition (13.7%) during the data collection and for this reason the standard reflections were measured every 150 reflections. Calculations were performed on standard PC 486/16MB.

Data collection: *CAD-4 Software* (Enraf–Nonius, 1989). Cell refinement: *CAD-4 Software*. Data reduction: *NRCVAX* (Gabe, Le Page, Charland, Lee & White (1989). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *SHELXL93* (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1971) and *PLUTON* (Spek, 1991). Software used to prepare material for publication: *SHELXL93*.

The financial support of the Ministry for Science and Technology, Republic of Slovenia is gratefully acknowledged.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1220). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O. & Taylor, R. (1983). *Acc. Chem. Res.* **16**, 146–153.
Enraf–Nonius (1989). *CAD-4 Software*. Version 5.0. Enraf–Nonius, Delft, The Netherlands.
Gabe, E. J., Le Page, Y., Charland, J.-P., Lee, F. L. & White, P. S. (1989). *J. Appl. Cryst.* **22**, 384–387.
Johnson, C. K. (1971). *ORTEP*II. Report ORNL-3794, revised. Oak Ridge National Laboratory, Tennessee, USA.
Kálmán, A. & Párkányi, L. (1980). *Acta Cryst.* B**36**, 2372–2378.

Majcen Le Maréchal, A., Robert, A. & Leban, I. (1993). *J. Chem. Soc. Perkin Trans.* 1, pp. 351–356.
Rosenfield, R. E. Jr, Parthasarathy, R. & Dunitz, J. (1977). *J. Am. Chem. Soc.* **99**, 4860–4862.
Sheldrick, G. M. (1985). *SHELXS86. Crystallographic Computing* 3, edited by G. M. Sheldrick, C. Krüger & R. Goddard, pp. 175–189. Oxford University Press.
Sheldrick, G. M. (1993). *SHELXL93. Program for the Refinement of Crystal Structures.* University of Göttingen, Germany.
Spek, A. L. (1991). *PLUTON. Molecular Graphics Program.* University of Utrecht, The Netherlands.

Acta Cryst. (1997). C**53**, 1679–1682

Trihydrate 1/1 Salt Between (*R*)-Carnitine Amide and (1*R*,3*S*)-Camphoric Acid

PASQUALE DE SANTIS,[a]* MERCEDES CAMALLI,[b] RICCARDO SPAGNA,[b] G. GALLO,[c] F. GIORGI[c] AND M. O. TINTI[c]

[a]*Dipartimento di Chimica, Università di Roma, 'La Sapienza', Piazzale Aldo Moro 5, I-00185 Roma, Italy,* [b]*Istituto di Strutturistica Chimica, 'G. Giacomello'–CNR, Area di Ricerca Montelibretti, Italy, and* [c]*Laboratori di Ricerca Chimica, Sigma-Tau, Pomezia, Italy. E-mail: pdesantis@caspur.it*

(*Received 10 July 1996; accepted 13 May 1997*)

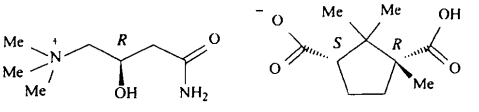
Abstract

The crystal structure of the trihydrate 1/1 salt between (*R*)-carnitine amide and (1*R*,3*S*)-camphoric acid, (*R*)-3-hydroxy-4-(trimethylammonio)butanamide (1*R*,3*S*)-1-carboxy-1,2,2-trimethyl-3-cyclopentanecarboxylate trihydrate, $C_7H_{17}N_2O_2^+.C_{10}H_{15}O_4^-.3H_2O$, is characterized by alternating layers of camphoric acid and carnitine amide molecules, both connected by a network of hydrogen bonds involving water molecules. Molecular-mechanics calculations using periodic boundary conditions, with two different force fields (*CVFF* and *AMBER*) and a dielectric constant ranging between 1 and 10, indicate that such commercial packages are not fully suitable when different kinds of forces are involved.

Comment

Carnitine and its derivatives are found to occur naturally in both plant and animal tissues, and in relatively high concentrations in the hearts and muscles of vertebrates (Fraenkel & Friedman, 1957; Hosein, Booth, Gasoi & Kato, 1967). The acetyl derivative is involved in carbohydrate metabolism (Childress, Sacktor & Traynor, 1966), as well as in the reversible transfer of the acetyl group between acetyl carnitine and acetyl coenzyme A. The acyl-carnitines play an important role in fatty acid oxidation by providing the transport of fatty acyl groups across mitochondria membranes (Colucci & Gandour, 1988). Acyl transfer is catalyzed by carnitine acyltransferase enzymes that comprise a family of proteins with different sub-cellular localization, substrate specificity and sensitivity to inhibitors (Bieber, 1988). In view of such properties, carnitine is useful in the therapeutic treatment of myocardial ischemia (Visioli, Pasini & de Giuli, 1992), acetylcarnitine is useful in cerebral aging and peripheral neuropathies (Calvani, 1993), while carnitine palmitoyl transferase inhibitors have potential therapeutic applications in the treatment of diabetes (McGarry, Woeltje, Kuwajima & Foster, 1989).

The study of the salts between (*R,S*)-carnitine derivatives and molecules or macromolecules capable of discriminating the two enantiomers can be useful to identify the topographical arrangement of the key recognition sites on carnitine binding enzymes, as well as to suggest alternative methods for stereoselective separation in analytical applications. Therefore, we have undertaken solid-state structural studies involving carnitine derivatives such as the title compound, (I), and protein moieties, in order to investigate the origin of the chiral discrimination of carnitine derivatives, as well as to provide a test of force-field models with respect to their adoption in theoretical calculations.



(I)

The crystal structure is characterized by alternate layers, nearly perpendicular to the *b* axis, of camphoric acid molecules and carnitine amide molecules connected by a network of hydrogen bonds involving the water molecules. Such a structure appears to be particularly stable as the same crystal cell parameters and X-ray diffraction data are obtained when the compound is recrystallized from isobutanol. The structure of the independent salt unit is shown in Fig. 1. Bond lengths and angles are as expected except for those involved in the camphoric rings that are reported in Table 1. Furthermore, consideration of the C—O bond lengths in the carboxyl groups allows assignment of the anion site to C17, in agreement with chemical evidence. Carnitine amide conformational parameters are very similar to those found in related carnitine derivatives (Gandour, Colucci & Fronczek, 1985; Colucci, Gandour & Mooberry, 1986). The molecule assumes an extended conformation even if an amide group replaces the carboxylate, or the counterion is different.

The packing in the *bc* plane, showing the hydrogen-bonding network, is illustrated in Fig. 2. The crystal structure is characterized by a three-dimensional