Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

Chelidamic acid monohydrate: the proton complex of a multidentate ligand

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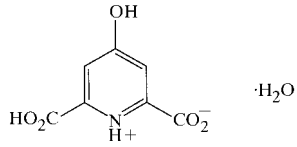
Received 14 May 1999
Accepted 1 December 1999

Chelidamic acid, 4-hydroxypyridine-2,6-dicarboxylic acid, is found to be zwitterionic in its solid monohydrate form, $C_7H_5NO_5\cdot H_2O$, with the aryloxide and one carboxylate group remaining protonated, but the other carboxylate group losing its proton to the pyridine N atom. In this, it is unlike its parent, dipicolinic acid (pyridine-2,6-dicarboxylic acid), which also crystallizes as a monohydrate, but one in which the acidic H atoms remain bound to the carboxylate groups. In both structures, the water molecule is a component of an extended hydrogen-bonded network.

Comment

Anions derived from weak protic acids form a very extensive family of metal-coordinating agents. In this regard, the acids themselves can be considered as precursive proton complexes, providing useful reference points for analysing the various effects that complexation may have on both metal and ligand properties. We have discussed this issue in recent structural studies of polynitrophenols and their derivatives (Harrowfield, Sharma, Shand *et al.*, 1998; Harrowfield, Sharma, Skelton & White, 1998; Harrowfield, Sharma, Skelton, Venugopalam & White, 1998), where aromatic π-stacking interactions seem to play an important role in determining coordination modes in the solid state. In extending this work to the study of heteroaromatic polycarboxylates, we have found the need to determine the crystal structure of chelidamic acid (4-hydroxypyridine-2,6-dicarboxylic acid, H_3chel), the source of a potentially trianionic chelating agent, though, in fact, only rather limited information is available on the nature of metal-bound chelidamate (Bag *et al.*, 1962; Thich *et al.*, 1976; Cline *et al.*, 1979; Pike *et al.*, 1983). We report here the structure of chelidamic acid, (I), comparing it with that known for the closely related dipicolinic acid (pyridine-2,6-dicarboxylic acid; Takusagawa *et al.*, 1973), also the parent of an important chelating anion (Harrowfield *et al.*, 1995, and references therein), in order to draw conclusions as to the sites and effects of proton residency within such molecules, as well as to assess the nature of factors influencing their solid-state structures.



(I)

The results of the low-temperature (*ca* 153 K) single-crystal X-ray study of chelidamic acid are consistent in overall stoichiometry and connectivity with formulation as the monohydrate, $C_7H_5NO_5\cdot H_2O$, one formula unit devoid of crystallographic symmetry comprising the asymmetric unit of the structure. Data quality permitted location and refinement of H atoms, showing the distribution of these is at variance with the conventional description of the acid as 4-hydroxypyridine-2,6-dicarboxylic acid, since it is in fact zwitterionic, with a cationic pyridinium centre balanced by the (under the present numbering) 2-carboxylate anion. Detailed molecular geometry is given in Table 1 in comparison with pyridine-2,6-dicarboxylic acid (Takusagawa *et al.*, 1973). Structural data for chelidamate derivatives in the literature concern a series of macrocycles in which the two carboxylate groups of chelidamic acid are esterified into an 18-membered ring (*R*OH = $C_{15}H_{19}NO_8$) which, in one case, is found with the aryloxide both protonated and deprotonated in separate moieties ($PhCH_2NH_3^+\cdot RO^-\cdot R$OH) (Bradshaw *et al.*, 1985), and in a further derivative, *R*OMe, has the aryloxide moiety methylated (Bradshaw *et al.*, 1985).

Within H_3chel itself, two sources of asymmetry exist. The aryloxide O atom is protonated and, as is the case with O*R*′ substituents appended to phenyl rings, the *R*′ (including H) groups tend to lie coplanar with the ring, with consequent asymmetry in the angles exocyclic at the point of attachment. Here, we find C4—O4 of a length comparable with counter-

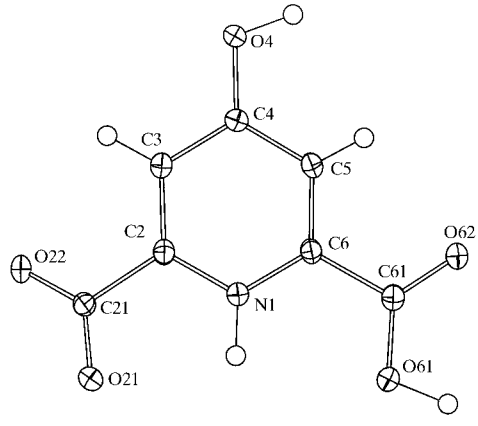


Figure 1
Projection of a single molecule normal to the ring plane, showing non-H atoms with 50% ellipsoids and the atom-labelling scheme.

part values in the *R*OH and *R*OMe species; in the latter, a considerable asymmetry in the associated exocyclic angles is observed which is unusually diminished in the present case. It is of interest to note that in the RO^- species, without any R' substituent, the angular asymmetry is greater, suggesting hydrogen bonding and other lattice forces to be appreciable, while the C4—O4 bond is appreciably shorter, with a greatly diminished endocyclic angle opposite it, in keeping with some enhancement of its double-bond character. The angle C3—C4—C5 is little different amongst the substituted phenoxide arrays relative to unsubstituted dipicolinic acid, though associated C4—C3,5 distances may be slightly shorter in the latter. The other source of asymmetry, not found in the other arrays, is the dissimilarity in the carboxylate groups, one being deprotonated and the other not. This appears to be of little consequence within the region bounded by the carboxylate C atoms other than some asymmetry in the exocyclic angles at C2; angular differences between C21 and C61 are minor, despite the difference in associated protonation and some differences in counterpart C—O bond lengths. Relative to the *ROR*′ arrays, however, large differences are noted in the latter in respect of C*n*—C*n*1—O*n*1,2 angles, C*n*1—O*n*2 being appreciably shorter and almost purely double bond in these species. In dipicolinic acid, interesting variations are also observed in the carboxylates; despite the protonation of both, the COH dispositions are relatively *cis* and *trans* to the ring nitrogen about the C*n*—C*n*1 bond, with concomitant changes in C*n*—C*n*1—O*n*1,2 comparability. In all these systems, as is usual, the carboxylate groups tend to lie coplanar with the aromatic ring, despite predominantly single-bond character in C*n*—C*n*1, but deviations from coplanarity are large, C_2O_2/C_5N interplanar dihedral angles often rising above 20° in the above systems. Protonation of the pyridine N atom in H_3chel is accompanied by enlargement of C2—N1—C6 relative to the unprotonated arrays; associated C—N distances are slightly lengthened. It is of interest to note that both H_2dipic and H_3chel crystallize as monohydrates, as also does *R*OH in isolation (Bradshaw *et al.*, 1985). In all cases, the water molecule is intimately involved in the hydrogen-bonding array but there appears to be no distinctive feature common to these systems explaining the monohydrate status. The siting of the water molecule in chelidamic acid hydrate directly above the centroid of an aromatic ring, for example, is not duplicated in dipicolinic acid hydrate. Hydrogen bonds found in the present array are described in Table 2, showing interactions from all NH or OH entities, those from the water H atoms, presumably the least acidic, being weakest; within the water molecule, H—O—H is 114 (2)°. Within the lattice, the H_3chel molecules lie quasi-normal to the *a* axis. Relatively close (3.3–3.6 Å) approaches between atoms within formally separate aromatic rings are found in all chelidamate and dipicolinate structures known and may be indicative of significant 'face-to-face' (π-stacking) and/or 'edge/vertex-to-face' aromatic group interactions (Harrowfield, 1996; Dance & Scudder, 1998, and references therein). In the hydrates of the acids in particular, hydrogen-bonded arrays form sheets which lie parallel to one another, approximately 3.4 Å apart.

Experimental

Crystals suitable for diffraction measurements were obtained by forming a saturated solution of chelidamic acid monohydrate (Aldrich) in boiling water, filtering out the solid rapidly precipitated on cooling to room temperature and then allowing the filtrate to evaporate slowly under ambient conditions. Small colourless tablets were readily obtained.

Crystal data

$C_7H_5NO_5·H_2O$
M_r = 201.13
Monoclinic, $P2_1/n$
a = 6.8832 (6) Å
b = 9.0568 (8) Å
c = 12.4376 (11) Å
β = 97.219 (2)°
V = 769.21 (12) Å^3
Z = 4
D_x = 1.737 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3552 reflections
θ = 1–28°
μ = 0.156 mm^{-1}
T = 153 K
Block, colourless
0.1 × 0.1 × 0.1 mm

Data collection

Bruker AXS CCD area-detector diffractometer
ω scans
8642 measured reflections
1962 independent reflections
1639 reflections with $F > 4\sigma(F)$
R_{int} = 0.031
θ_{max} = 28.87°
$h = -9 \rightarrow 9$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 16$

Table 1
Comparative geometries (Å,°).

	H_2dipic	H_3chel
N1—C2	1.338	1.357 (2)
N1—C6	1.336	1.354 (2)
C2—C3	1.398	1.378 (2)
C5—C6	1.388	1.366 (2)
C3—C4	1.370	1.403 (2)
C4—C5	1.380	1.398 (2)
C4—O4	—	1.331 (2)
C2—C21	1.507	1.518 (2)
C6—C61	1.512	1.510 (2)
C21—O21	1.217	1.260 (2)
C61—O61	1.181	1.295 (2)
C21—O22	1.289	1.244 (2)
C61—O62	1.314	1.221 (2)
C2—N1—C6	116.7	120.0 (1)
N1—C2—C3	123.4	121.2 (1)
N1—C6—C5	123.3	121.2 (1)
C2—C3—C4	119.0	119.2 (1)
C4—C5—C6	119.3	120.0 (1)
C3—C4—C5	118.3	118.4 (1)
C3—C4—O4	—	119.8 (1)
C5—C4—O4	—	121.8 (1)
N1—C2—C21	118.4	117.3 (1)
N1—C6—C61	115.3	120.4 (1)
C3—C2—C21	118.2	121.4 (1)
C5—C6—C61	121.4	118.4 (1)
C2—C21—O21	116.3	115.9 (1)
C6—C61—O61	124.8	115.5 (1)
C2—C21—O22	119.3	116.2 (1)
C6—C61—O62	110.8	118.1 (1)
O21—C21—O22	124.4	127.9 (1)
O61—C61—O62	124.4	126.4 (1)
Interplanar dihedral angles		
$O_2C_2(2)/C_5N$	6.0	23.18 (5)
$O_2C_2(6)/C_5N$	4.0	6.86 (5)

Refinement

Refinement on F	All H-atom parameters refined
$R = 0.038$	$w = 1/[\sigma^2(F) + 0.004F^2]$
$wR = 0.049$	$(\Delta/\sigma)_{max} = 0.041$
$S = 1.736$	$\Delta\rho_{max} = 0.31$ e Å^{-3}
1639 reflections	$\Delta\rho_{min} = -0.26$ e Å^{-3}
156 parameters	

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

D—H···A	D—H	H···A	D—H···A
N1—H1···O01^{i}	0.98 (2)	1.74 (2)	169 (2)
O4—H4···O22^{ii}	0.99 (2)	1.61 (2)	168 (2)
O61—H61···O21^{iii}	1.03 (2)	1.46 (2)	172 (2)
O01—H01*a*···O4^{i}	0.94 (3)	1.99 (3)	169 (2)
O01—H01*b*···O62^{iv}	0.90 (3)	1.88 (3)	167 (2)

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

Data collection: *SMART* (Siemens, 1995); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *Xtal*3.5 *GENTAN* (Hall *et al.*, 1995); program(s) used to refine structure: *Xtal*3.5 *CRYLSQ*; molecular graphics: *Xtal*3.5 *PIG ORTEP*; software used to prepare material for publication: *Xtal*3.5 *BONDLA CIFIO*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: CF1322). Services for accessing these data are described at the back of the journal.

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