Carbacylamidophosphates: Structure and Properties of Bis(N,N'-morpholido)-[(N''-morpholido)-carboxamido] phosphate

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The bis(N,N'-morpholido)-[(N''-morpholido)-carboxamido] phosphate: O(2CH2CH2)NC(O)-N(H)P(O)[N(CH2CH2)O]2 [HL], has been prepared and characterized by means of IR, 31P and 1H NMR spectroscopy and X-ray diffraction (triclinic, a = 9.282(2), b = 9.308(2), c = 21.341(4) Å, α = 80.79(3)°, β = 80.92(3)°, γ = 66.92(3)°, V = 1665.1(6) Å3, space group P1, Z = 4 and R = 0.0423, wR2 = 0.1303 for 6774 unique reflections used). The unit cell consists of two independent molecules connected by hydrogen bonds N-H...O=P into non-symmetric dimers. The compound behaves as a HL molecule with a protonation constant corresponding to the -C(O)N(H)P(O)- group of pK = 8.65 as determined by potentiometric studies.

Introduction

Compounds of formula R=C(O)NHP(O)R' are PN-analogues of β-diketones and also potential bidentate O,O-donor ligands for metal ions [1]. Many of the phosphazo analogues of β-diketones including the chelate group -C(O)N(=)P-O= possess bioactivity and are used in clinical practice as anti-cancer drugs [2, 3].

The X-ray structures of some carbacylamido-phosphates have been determined [4 - 6]. The results have shown that in the molecular core unit -C(O)N(H)P(O)= the C=O and P=O oxygen atoms are in anti- positions to each other, and that the C=C(O)N- unit is virtually planar.

This work reports the results of the X-ray investigation of the structure of (HL).

Experimental

Preparation and identification of bis(N,N'-morpholido)-[(N''-morpholido)-carboxamido] phosphate was carried out as described previously [7]. Single crystals for X-ray investigations were obtained by recrystallization from isopropanol. The IR spectra of HL were recorded on a UR-10 spectrometer (400 - 4000 cm⁻¹) in KBr pellets. 1H and 31P NMR spectra were recorded on a Bruker WP-100SY spectrometer at room temperature in methanol-d₄ solutions.

For the X-ray diffraction study a crystal of the dimensions 0.3 x 0.25 x 0.2 mm was used. Crystallographic measurements were carried out on a Kuma KM4CCD diffractometer with graphite monochromated Cu-Kα radiation at 20 °C. Table I lists the cell parameters and details of the data acquisition and structure refinement. The structure was solved by direct methods and subsequent Fourier difference techniques for all non-hydrogen atoms and refined using the programs SHELXS-86 and SHELXL-93 [8, 9]. All hydrogen atoms were calculated based on the geometry of the molecules. Convergence was reached at the R-values given in Table I. The principal interatomic distances and angles are given in Table II. Full structure data have been deposited at the Cambridge Crystallographic Data Centre [10].

Results and Discussion

The crystals of HL are composed of non-centrosymmetric dimers (HL)₂ (Fig. 1). Molecules are linked via hydrogen bonds formed by phosphorlyc oxygen atoms and hydrogen atoms of amide groups. The parameters of the hydrogen bond are typical for dimers of carbacylamidophosphates (Table III). Both molecules are not only nearly identical in their distances and angles but also in their configuration. Small differences in the angles and torsion angles may be attributed to intermolecular interactions.

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The configuration at the P atom is that of a distorted tetrahedron, and only the angles O(1)-P(1)-N(1) of 105.80(9)° in molecule I, and O(2)-P(2)-N(2) of 106.20(9)° in molecule II, are smaller than normal [11].

The surroundings of the nitrogen atoms of the morpholinic groups, N(31) and N(61) for molecule I and II, respectively, are nearly planar (the sum of angles is 359° in both cases). The nitrogen atoms of the other morpholinic groups have more significant deviations from trigonal with sums of the angles (352° for N(11) and 353.53° for N(21), in molecule I, and 351.6° for N(41) and 353.32° for N(51) in molecule II).

The bond distances P(1)-O(1) = 1.4762(15) Å (in molecule I) and P(2)-O(2) = 1.4743(16) Å (in molecule II) are typical for compounds with amide substituents close to phosphorus atoms (1.465 - 1.482 Å) [11].

The bond lengths C(1)-O(1') 1.223(2), C(2)-O(2') 1.222(2), C(1)-N(1) 1.380(2) and C(2)-N(2) 1.381(2) are similar to analogues having etheric substituents at phosphorus atom, but longer than for trichloracetylamidophosphates [4, 5, 12, 13].
In the structure of HL the carbonyl and phosphoryl groups are in an anti-position to each other as in most of the carbacylamidophosphates.

All the morpholine rings are in a chair conformation.

The environment of the C(1), C(2) atoms is nearly planar (the deviations from the root-mean-square planes through the atoms O(1'), N(1), N(11), C(1) in molecule I and O(2'), N(2), N(41), C(2) in molecule II do not exceed 0.001 Å).

The carbonyl oxygen – phosphorus distances (3.001 Å in I, 3.011 Å in II) are considerably less then the sum of their van-der-Waals radii (3.30 Å) and represent a close contact between the nucleophilic oxygen and electrophilic phosphorus atoms.

In the $^{31}$P NMR spectrum the signal lies at 12.2 ppm, typical for phosphotriamides.

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