



SYNTHESIS, SPECTROSCOPIC CHARACTERIZATION, CRYSTAL STRUCTURE AND HIRSHFELD SURFACE ANALYSIS OF (4-Cl-C₆H₄O)(OC₄H₈N)₂PO AMIDOPHOSPHOESTER

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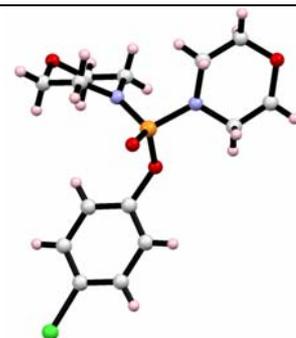
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A new amidophosphoester, (4-Cl-C₆H₄O)(OC₄H₈N)₂PO, was synthesized and characterized by spectroscopic methods (IR, ³¹P-, ¹³C-, ¹H-NMR) and single-crystal X-ray diffraction. The crystal belongs to the space group *P2₁/c*, and the asymmetric unit of structure is composed of one complete molecule. The P atom has a distorted tetrahedral (O)(N)₂P(O) environment with one of the O=P—N angles as the maximum angle at the P atom and one of the O—P—N angles as the minimum angle. The oxygen atom of the P—O—C₆H₄-4-Cl part may be ascribed with the hybridization including a few more “s” character with respect to “sp²”, reflected in the P—O—C angle (127°). In the crystal, the molecules are aggregated through CH...O hydrogen bonds forming a two-dimensional array along the *bc* plane.



INTRODUCTION

The term “amidophosphoester” denotes compounds which dually contain (RO)P=O part (R = a hydrocarbon group) with together an R¹R²N group bonded to phosphorus through nitrogen (R¹ and R² = H or a hydrocarbon group); viz. the compounds typically with the (RO)₂(R¹R²N)P(O) or (RO)(R¹R²N)₂P(O) formulas.^{1,2} The extensive investigations on the biochemical properties of amidophosphoesters revealed various possibilities for their application in preparation of different classes of drugs, insecticides and pesticides.³⁻⁵ Some amidophosphoesters are well-known as inhibitor of acetylcholinesterase (AChE) enzyme, which is responsible for the degradation of acetylcholine, a neurotransmitter involved in the process of learning

and memory.^{6,7} Moreover, anti-human immunodeficiency virus efficacies of some derivatives were reported.⁸ Besides the biological activities of amidophosphoesters, some of them were used as oxygen-donor ligands in coordination chemistry⁹ and as flame-retardant compounds in polymer additives.¹⁰

Amidophosphoesters are also interesting for pure scientific studies, like for example in NMR considerations and investigation of phosphorus-hydrogen and phosphorus-carbon coupling constants^{11,12} and crystallography experiments, typically for (RO)(R¹R²N)₂P(O) amidophosphoesters with RO = C₆H₅O¹³ and 4-CH₃-C₆H₄O.¹⁴

A survey on the Cambridge Structural Database (CSD)¹⁵ revealed that one cation-anion amidophosphoester with RO = 4-Cl-C₆H₄O has been reported so far (CSD refcode FIYXOA)¹⁶ and in this paper we

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report the first neutral structure (studied by X-ray crystallography) with the same aryloxy group, (4-Cl-C₆H₄O)(OC₄H₈N)₂PO (Fig. 1). The phosphorus chemical shift and ²J_{C-P} and ³J_{C-P} coupling constants of this amidophosphoester are compared with the previously reported analogous compounds.

RESULTS AND DISCUSSION

Spectroscopic features

In the ³¹P{¹H} NMR spectrum, the phosphorus signal appears at the chemical shift of 10.02 ppm as a singlet (in DMSO-d₆), in comparison with a published analogous compound C₆H₅OP(O)(NH)₂C₅H₁₀ with the value of 7.56 ppm in the same solvent.¹⁷ We also bring an example including the OC₄H₈N group belonging to the phosphoric triamide family, *i.e.* (4-NO₂-C₆H₄NH)(OC₄H₈N)₂P(O), with its phosphorus signal in a chemical shift very close to that in the title compound (9.99 ppm in DMSO-d₆).¹⁸ In the ¹H NMR spectrum, the multiplets at the aliphatic regions for axial and equatorial hydrogen atoms and two doublets at aromatic region are revealed as expected. For the OC₄H₈N group, the doublet signal at 66.75 ppm (³J_{C-P} = 5.8 Hz), in ¹³C NMR, is assigned to the carbon atom with three bonds separation from phosphorus, while the carbon signal at 44.78 ppm appears as a singlet. The data for the signals of NC₄H₈O ring in the title compound are also comparable with those in (4-NO₂-C₆H₄NH)(OC₄H₈N)₂P(O) phosphoric triamide, *i.e.* a doublet at 66.87 ppm (*J* = 5.7 Hz) and a singlet at 44.72 ppm. The two carbon atoms of 4-Cl-C₆H₄O group with two and three bonds separations with respect to phosphorus reveal as doublets, at 150.18 ppm (²J = 5.7 Hz) and at 128.97 ppm (³J = 13.2 Hz), respectively. In the IR spectrum, the band at 1274 cm⁻¹ is attributed to the P=O stretching frequency.

Description of the crystal structure

The crystallographic data and details of the X-ray analysis are presented in Table 1 and selected bond distances and angles are given in Table 2. The asymmetric unit of the title structure is composed of one complete molecule, as shown in Fig. 2.

The P=O, P—N and P—O bond lengths are within the expected ranges of those in analogous amidophosphoesters. The P atom has a distorted tetrahedral (O)(N)₂P(O) environment, with one of the O=P—N angles as the maximum angle at the P atom (O2-P1-N2 = 122.0(3)°) and one of the O—P—N angles as the minimum angle (O1-P1-N2 = 103.7(3)°).

The bond-angle sum of 359.5° for N1 (C—N—C + 2 P—N—C) confirms its *sp*² character or a planar geometry at this nitrogen atom. The other nitrogen atom (N2) has a bond-angle sum of 350.4°, showing the more pronounced *p* character of the orbitals (with respect to the *sp*² and toward *sp*³). The criteria for distinguishing between planar and non-planar geometries from bond-angle sums were defined in a previously published paper: N(planar) and N(pyramidal) refer to the cases with Σ ≥ 352.5° and Σ ≤ 339.0°, respectively, and the intermediate entries are the cases with Σ in the range 339.0° – 352.5°.¹⁹ The P—N bonds made by these two nitrogen atoms are different and the nitrogen atom within a planar environment makes a shorter P—N bond (P1-N1 = 1.575(6) and P1-N2 = 1.760(6) Å). Furthermore, at both tertiary N atoms, the C—N—C angle is smaller than the two C—N—P angles. The orientation of the atoms attached to the non-planar N atom corresponds to an anti-orientation of the corresponding lone electron pair (LEP) with respect to the P=O group.

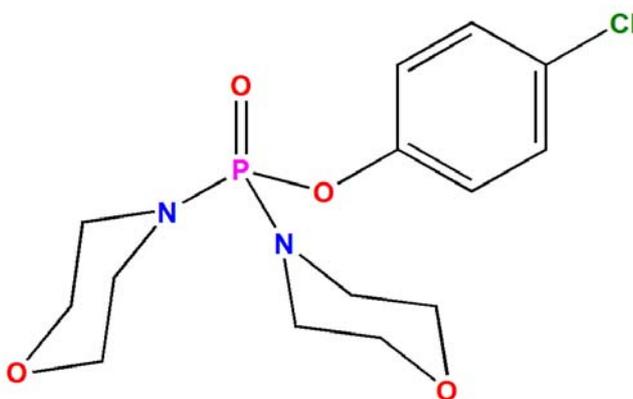


Fig. 1 – Chemical structure of title amidophosphoester.

Table 1

Crystallographic data, details of data collection and structure refinement

Chemical formula	C ₁₄ H ₂₀ ClN ₂ O ₄ P
M _r	346.74
Crystal system, space group	Monoclinic, <i>P</i> 2 ₁ / <i>c</i>
Temperature (K)	293(2)
<i>a</i> , <i>b</i> , <i>c</i> (Å)	11.693(2), 9.3237(19), 15.828(6)
β (°)	105.48(2)
<i>V</i> (Å ³)	1663.0(8)
<i>Z</i>	4
<i>D</i> _x (g.cm ⁻³)	1.385
Mo <i>K</i> α radiation	λ = 0.71073 Å, μ = 0.344 mm ⁻¹
Crystal size (mm)	0.28 × 0.22 × 0.12
θ range for data collection	2.67–20.81°
No. of reflections	1386
No. of measured	5124
<i>R</i> _{int}	0.0783
Data/restraints/parameters	1699/0/199
Goodness-of-fit on <i>F</i> ²	1.118
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²)	0.0803, 0.1707
<i>F</i> (000)	728
(Δ/σ) _{max} < 0.001	Δρ _{max} = 0.348 e Å ⁻³ , Δρ _{min} = -0.243 e Å ⁻³

Table 2

Selected bond lengths (Å) and angles (°)

P1-O1	1.644(5)	O4-C10	1.410(10)
P1-O2	1.360(4)	O4-C11	1.552(11)
P1-N1	1.575(6)	N1-C8	1.351(8)
P1-N2	1.760(6)	N1-C5	1.457(8)
O1-C4	1.543(8)	N2-C12	1.477(9)
O3-C6	1.330(9)	N2-C9	1.573(9)
O3-C7	1.401(9)	C11-C1	1.930(7)
O2-P1-N1	108.0(3)	C10-O4-C11	108.2(7)
O2-P1-O1	106.2(3)	C8-N1-C5	110.6(6)
N1-P1-O1	112.6(3)	C8-N1-P1	120.9(5)
O2-P1-N2	122.0(3)	C5-N1-P1	128.0(5)
N1-P1-N2	104.5(3)	C12-N2-C9	106.9(6)
O1-P1-N2	103.7(3)	C12-N2-P1	119.8(5)
C4-O1-P1	127.0(4)	C9-N2-P1	123.7(4)
C6-O3-C7	109.3(6)	C2-C1-C11	122.7(6)

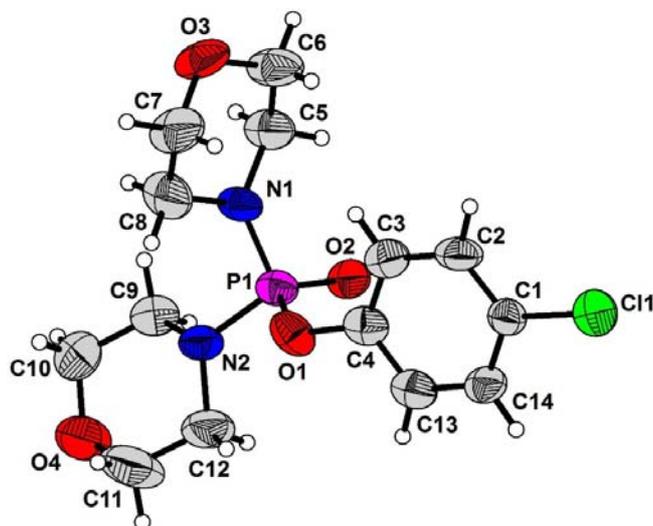


Fig. 2 – Displacement ellipsoid plot (50% probability level) and the atom numbering scheme for (4-Cl-C₆H₄O)(OC₄H₈N)₂PO. H atoms are shown as circles of arbitrary radii.

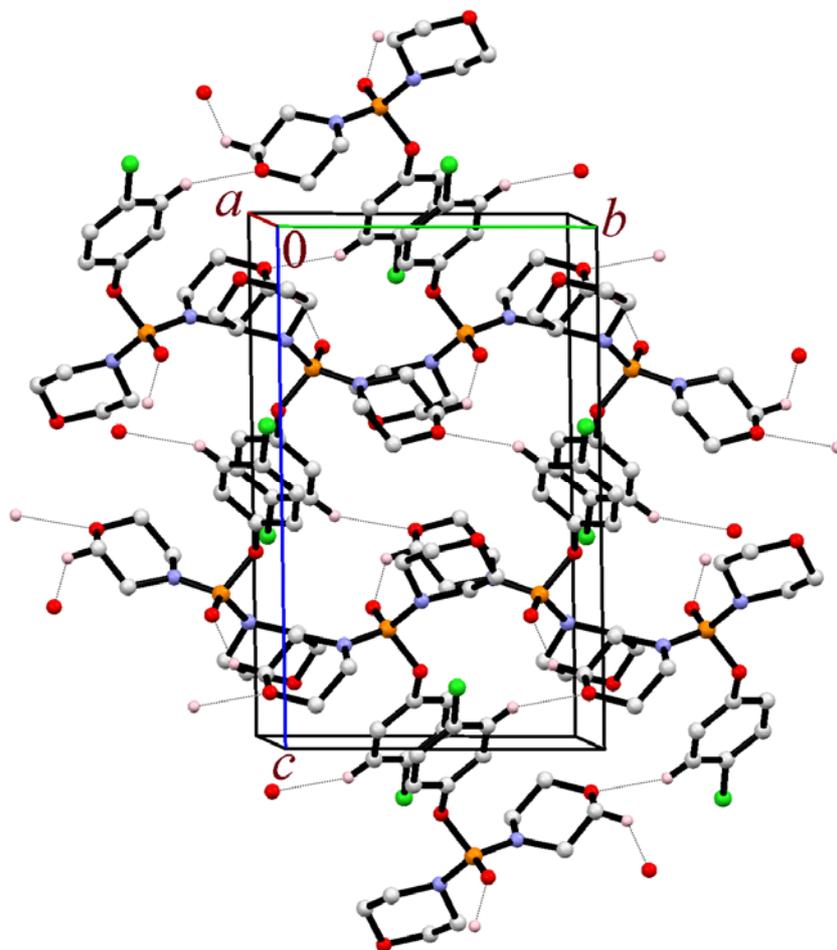


Fig. 3 – A view of two-dimensional array of the title structure along the bc plane.

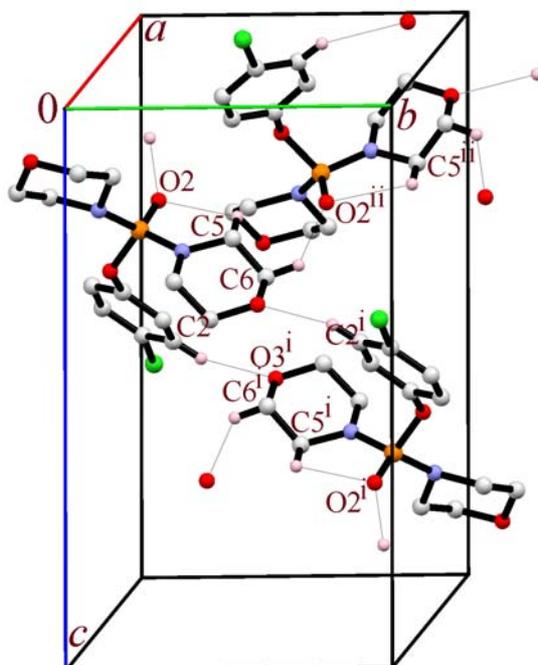


Fig. 4 – Part of the crystal packing of $(4\text{-Cl-C}_6\text{H}_4\text{O})(\text{OC}_4\text{H}_8\text{N})_2\text{PO}$ showing $\text{CH}\dots\text{O}$ hydrogen bonds (as dotted lines), symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $1-x, 1/2+y, 1/2-z$. The hydrogen atoms that are not involved in hydrogen bonds were omitted for clarity.

Table 3

Hydrogen bond geometries (e. s. d. s given in parentheses)

$D-H...A$	$D-H$ (Å)	$H...A$ (Å)	$D...A$ (Å)	$\angle D-H...A$ (°)
C2-H2...O3 ⁱ	0.93	2.52	3.275(10)	139
C5-H5A...O2	0.97	2.46	2.903(9)	108
C6-H6B...O2 ⁱⁱ	0.97	2.37	3.015(11)	124

Symmetry codes: (i) $1-x, 1-y, 1-z$; (ii) $1-x, 1/2+y, 1/2-z$.

The oxygen atom of the P—O—C₆H₄-4-Cl part may be ascribed with the hybridization including a few more “s” character with respect to “sp²”, reflected in the P—O—C angle of 127.0(4)°. This is in accordance with the result of a CSD analysis for compounds with (O)₂(N)P(O) and (O)₂(N)P(S) skeletons and containing at least one C—O—P bond,² which is also relevant for a structure with an (O)(N)₂P(O) skeleton such as the title compound.

In the crystal, the molecules are aggregated through CH...O hydrogen bonds forming a two-dimensional array along the *bc* plane (Fig. 3). In this arrangement, each molecule is surrounded with four neighbouring molecules through the hydrogen bonds noted. In this hydrogen bond pattern, the oxygen atom of phosphoryl group and the oxygen atom of one NC₄H₈O group take part as hydrogen bond acceptors, as shown in Fig. 4.

Hirshfeld surface analysis and fingerprint plots

The Hirshfeld surface analysis, which uses three-dimension (3D) surfaces functions, as well as two-dimension (2D) fingerprint plots,^{20,21} is a very useful graphical tool for identification and understanding of intermolecular interactions within a crystal structure. The Hirshfeld surface mapped with d_{norm} and corresponding shape index associated 2D fingerprint plots of the title structure

were generated using the *Crystal Explorer* software version 3.1,²² with the structure file in the CIF format as the input.

Three large red areas can be seen in the surface, which correspond to two intermolecular C—H...O hydrogen bonds (labels 1 and 5 in Fig. 5), as noted in the crystal structure section, and one C—H... π interaction (label 3). Furthermore, the crystal shows a near H...H contact (label 2), a weak C—H...Cl contact (label 4) and two weak C—H...O contacts (labels 6 and 7), shown as small and pale red spots (Fig. 5).

In order to picture contacts in the crystal packing, the two-dimensional fingerprint plot was generated (Fig. 6). The full plot was also divided to the figures illustrating different contacts observed in the crystal (Fig. 7). According to divided fingerprints, the major frequently occurring contacts are the H...H and then the O...H/H...O contacts with the contribution portions of 48.7% and 20.1%, respectively. The other contacts in the crystal are Cl...H/H...Cl (15.7%), C...H/H...C (11.4%) and O...C/C...O (2.5%), and also some others with contribution portions below 1% (Cl...C/C...Cl, Cl...O/O...Cl, C...C and Cl...Cl). Furthermore, in the fingerprint plot, the H...H and H...O contacts respectively develop one and two nearly sharp spikes that are indicative of closest interactions in the crystal.

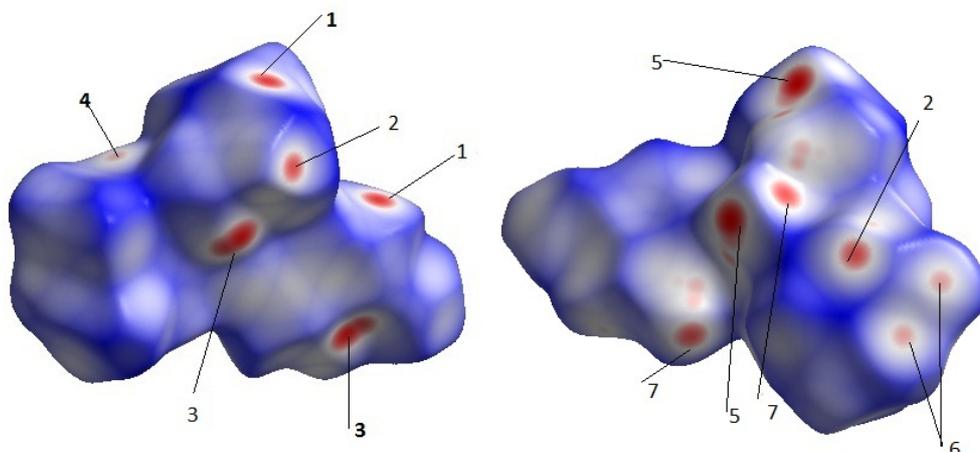
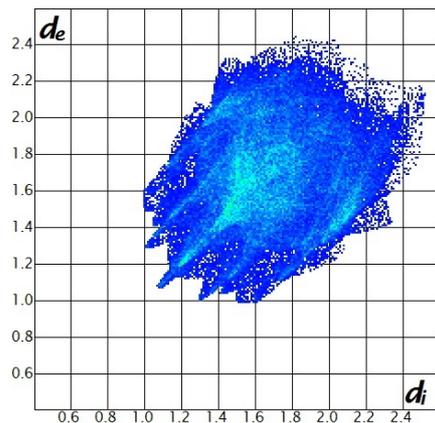
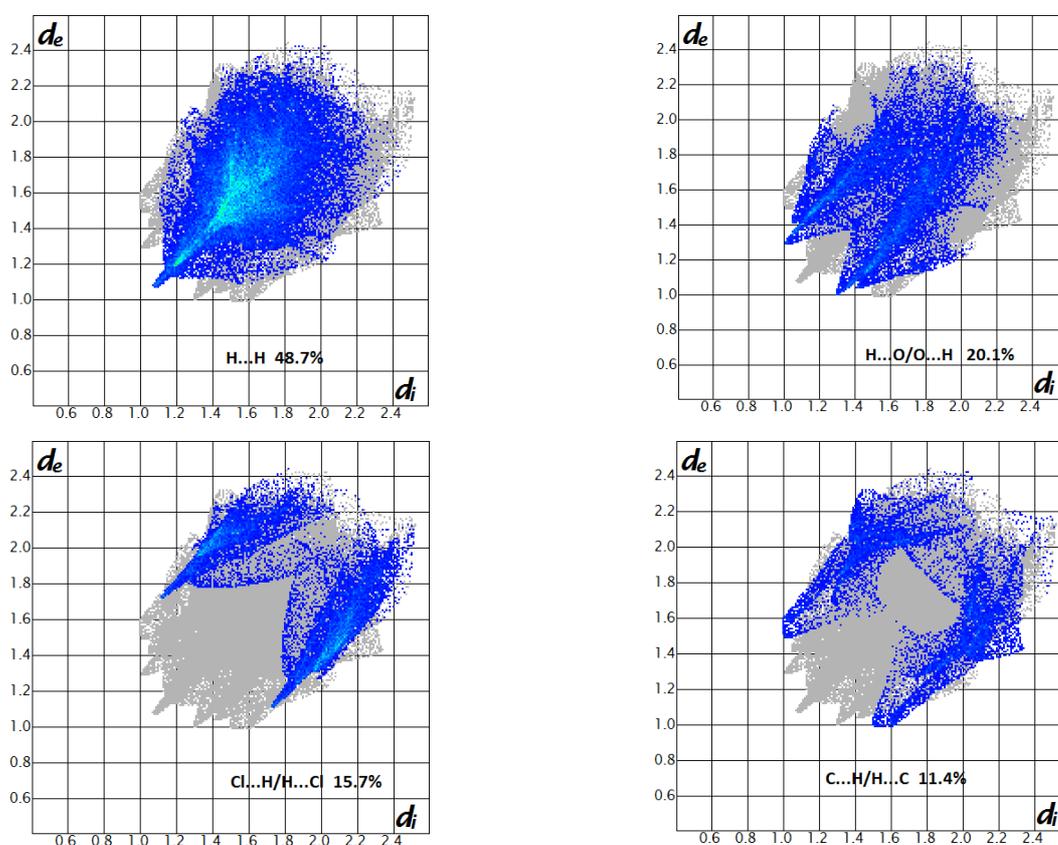


Fig. 5 – Front and back views of the Hirshfeld surface for (4-Cl-C₆H₄O)(OC₄H₈N)₂PO. The interactions according to the labels in the figures are as follows, with the labels in parentheses: C2-H2...O3 (1), H9B...H7A (2), C8-H8A...C14 (3), C9-H9A...C11 (4), C6-H6B...O2 (5), C10-H10B...O4 (6), C13-H13...O2 (7).

Fig. 6 – Full fingerprint plot for (4-Cl-C₆H₄O)(OC₄H₈N)₂PO.Fig. 7 – Divided fingerprint plots for (4-Cl-C₆H₄O)(OC₄H₈N)₂PO: H...H (top-left), O...H/H...O (top-right), Cl...H/H...Cl (bottom-left) and C...H/H...C (bottom-right).

EXPERIMENTAL

Materials and instrumentation

The chemicals were purchased from Aldrich and Merck with high purity. Infrared spectrum was recorded in a KBr disc on a Perkin-Elmer 78 spectrophotometer. ¹H, ¹³C and ³¹P NMR spectra were recorded on a Bruker Avance 250 MHz spectrometer. The chemical shifts were determined relative to TMS for ¹H and ¹³C and to 85% H₃PO₄ for ³¹P, as external standard. The X-ray data were collected at 293 K on a Mar 345 dtb image plate detector with graphite monochromated Mo K α radiation and solved by the direct methods algorithm

of SHELXS97 and refined by SHELXL97.²³ All hydrogen atoms were included in the refinement at geometrically fixed positions and refined with a riding model. The molecular graphics were generated by MERCURY²⁴ and the DIAMOND²⁵ for Windows program.

Synthesis of O-(4-chloro-phenyl), N-bis(morpholin-4-ylamido)phosphinate, (4-Cl-C₆H₄O)(OC₄H₈N)₂PO

The synthesis for the preparation of title compound began with the reagents being combined at ice-bath temperature and the mixture then allowed coming to room temperature for the

rest of the procedure. For the synthesis, a solution of $\text{OC}_4\text{H}_8\text{NH}$ (8 mmol) in CHCl_3 (10 ml) was added to a solution of $(4\text{-Cl-C}_6\text{H}_4\text{O})(\text{Cl})_2\text{PO}$ (2 mmol) in the same solvent (10 ml) at 273 K. After stirring for 4 h, the solvent was removed *in vacuo* to obtain a solid which was washed with distilled water. Single crystals suitable for X-ray crystallography were obtained from a solution of compound in CHCl_3 and then adding n-heptane (4:1 v/v) by slow evaporation at room temperature. IR (KBr, ν , cm^{-1}): 2960, 2931, 2860, 1728, 1488, 1462, 1274, 1123, 1073, 960, 874, 744. $^{31}\text{P}\{^1\text{H}\}$ NMR (DMSO-d_6): 10.02. ^{13}C NMR (DMSO-d_6): 44.78, 66.75 (d, $J = 5.8$ Hz), 128.97 (d, $J = 13.2$ Hz), 130.00, 131.94, 150.18 (d, $J = 5.7$ Hz). ^1H -NMR (DMSO-d_6): 0.84–1.61 (m, 4H), 3.07–4.12 (m, 12H), 7.24 (d, $J = 7.5$ Hz, 2H), 7.42 (d, $J = 8.0$ Hz, 2H).

CONCLUSIONS

In this work, amidophosphoester, $(4\text{-Cl-C}_6\text{H}_4\text{O})(\text{OC}_4\text{H}_8\text{N})_2\text{PO}$, was synthesized and characterized by spectroscopic methods and single crystal X-ray determination. The P atom in the molecule has a distorted tetrahedral $(\text{O})(\text{N})_2\text{P}(\text{O})$ environment, with difference between the maximum and minimum angles at phosphorus atom is more than 18° . In the crystal, the $\text{CH}\cdots\text{O}$ hydrogen bonds assemble the molecules in a two-dimensional array, where the oxygen atom of phosphoryl group and the oxygen atom of one $\text{NC}_4\text{H}_8\text{O}$ group take part as hydrogen bond acceptors, while the esteratic oxygen atoms does not take part in hydrogen bonding. The details analysis by Hirshfeld surface approach, with considering fingerprint plots, show besides the $\text{CH}\cdots\text{O}$ contacts the $\text{H}\cdots\text{H}$, $\text{H}\cdots\text{Cl}$ and $\text{H}\cdots\text{C}$ contacts participate in the crystal cohesion.

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