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Synthesis and Crystal Structure of [(2-Substituted phenylamino)(2-hydroxyphenyl)methyl]-phosphonic acid Diethyl Esters

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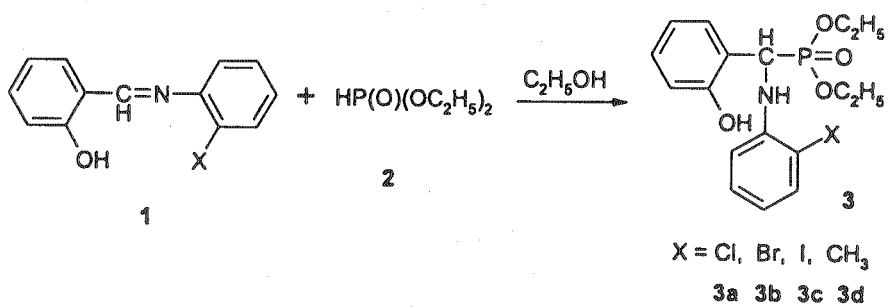
Novel derivatives of [(2-substituted phenylamino)(2-hydroxyphenyl)-methyl]phosphonic acid diethyl ester were sysnthesized by addition of diethyl phosphonate to corresponding Schiff bases. The structures of these derivatives have been elucidated on the basis of elemental analyses, IR, NMR and single crystal X-ray diffraction. The [(2-chlorophenylamino)(2-hydroxyphenyl)methyl]phosphonic acid diethyl ester, $C_{17}H_{21}NO_4PCl$ (3a) crystallize in monoclinic space group $P2_1/a$ with unit cell dimensions a = 8.0171(12), b = 33.0519(11), c = 15.1195(13) Å, β = 99.859(3) V = 3947.2(7) Å^3, Z = 4.

Key Words: Phosphonic acid diethyl esters, X-ray structure, Schiff bases.

INTRODUCTION

It's known that α-aminomethylphosphonic acids are antifungal[1] and antibacterial agents[2], as well as having strong chelating properties[3]. Synthesis of water soluble derivatives[4–6] and preparation of metal complexes of these compounds are great industrial interest[7]. In this study, the explanation of the structures and synthesis of the [(2-substituted phenylamino)(2-hydroxyphenyl)methyl]phosphonic acid diethyl esters (3), derived from the reaction of diethylphosphonate (2) with suitable Schiff bases (1), are reported (**Scheme-1**). The X-ray crystal structure of the [(2-chlorophenylamino)-(2-hydroxyphenyl)methyl]phosphonic acid diethyl ester (3a) is described.



Scheme-1. Synthesis of phosphonic acid diethyl esters

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EXPERIMENTAL

Melting points were determined with a Gallenkamp apparatus without correction. The elemental analyzer was LECO CHNS-932 instrument. IR spectra were run on a Mattson-1000 FTIR spectrometer using KBr pellets in the range 4000– 400 cm^{-1}. ^1H NMR spectra were recorded in $CDCl_3$ on a Bruker DPX 400 FT-NMR spectrometer with TMS as internal standard. The X-ray diffraction intensity data were collected at room temperature using an Enraf-Nonious CAD4 diffractometer with MoK_α (λ = 0.71073 Å) radiation in $\omega/2\theta$ scan mode. The cell parameters were determined from least-squares refinemet of 25 centred reflections in the ranges of $10.33 \leq \theta \leq 18.030$ (**3a**). Three standard reflections for every 120 min were periodically measured during data collection and showed no significant intensity varations. The structures were solved by direct methods using the solution program SHELXS 97[8a] and refined using SHELXL97[8b] in the WinGX[9] package. All non-hydrogen atoms were refined, first with isotropic and then with anisotropic thermal displacement parameters by full matrix least squares. All the hydrogen atoms were placed geometrically and were refined as riding with $U_{iso}(H) = 1.2\ U_{eq}(C, N, O)$. The hydrogen atoms of the crystal water were placed from difference map and were refined as riding with $U_{iso}(H) = 1.2\ U_{eq}(O)$ and $U_{iso}(H) = 1.5\ U_{eq}(C)$ for CH_3 group. The crystal and experimental data are given in Table-1.

TABLE-1
CRYSTAL AND EXPERIMENTAL DATA of **3a**

Chemical formula	$C_{34}\ H_{46}\ Cl_2\ N_2\ O_{10}\ P_2$
Formula weight	775.57
Crystal system, space group	Monoclinic, $P2_1/a$
Unit cell dimensions: (Å, 0)	
a	8.0171 (12)
b	33.0519 (11)
c	15.1195 (13)
β	99.859 (3)
Volume ($Å^3$)	3947.2 (7)
Z	4
Calculated density (g cm^{-3})	1.305
Absorption coefficient (mm^{-1})	0.30
F(000)	1632
Crystal size (mm)	0.15 × 0.20 × 0.25
Θ_{max} (°)	25.20
Index range	$-9 \leq h \leq 0, 0 \leq k \leq 39, -17 \leq l \leq 18$
Number of reflections used	6696
Number of parameters	452
R_{int}	0.017
R	0.058
R_w	0.148
Goodness of fit	1.01
$\Delta\rho_{min}, \Delta\rho_{max}$ ($eÅ^{-3}$)	–0.49, 0.67
Deposition number	CCDC 210015

Aldehydes and amines were obtained from Merck-Schuchardt AG. Diethyl phosphonate was a 98% product of Riedel de Haën. These chemicals were used without further purification. Freshly distilled ethanol (95%) was used as solvent.

Preparation of the Schiff Bases

Hot methanolic solution of equimolar amounts of amines [2-chlorophenylamine, 1.27 g, 0.01 mol; 2-bromophenylamine, 1.72 g, 0.01 mol; 2-iodophenylamine, 2.19 g, 0.01 mol; 2-methylphenylamine, 1.07 g, 0.01 mol] and salicylaldehyde (1.22 g, 0.01 mol) were mixed and allowed to stand overnight. The Schiff bases were obtained as yellow crystals of reaction mixture. Yields are over 90%. $C_{13}H_{10}NOC$: m.p. 84°C; IR (neat, cm^{-1}) 1618 s ν(C=N).m.f. $C_{13}H_{10}NOBr$; m.p. 90°C; IR (neat, cm^{-1}) 1614 s ν(C=N). m.f. $C_{13}H_{10}OI$; m.p. 53–54°C. IR (neat, cm^{-1}) 1612 s ν(C=N). m.f. $C_{14}H_{13}NO$; m.p. 50°C. IR (neat, cm^{-1}) 1618 s ν(C=N).

General procedure for synthesis of phosphonic acid diesters (3a–d)

A 10 mL ethanolic solution of 1.38 g (0.01 mol) diethyl phosphonate was added dropwise into the stirred solution of an equimolar amount of the Schiff base in 70 mL of ethanol. After the dropwise addition was completed, the mixture was refluxed for 24 h with constant stirring. The volatile substances were removed on a rotary evaporator. The oily residue was dissolved in 10–15 mL ethanol and set aside for crystallization. TLC was performed to follow the reaction as well as to determine the optimum reaction time.

$C_{17}H_{21}NO_4PCl$ **(3a):** Yield 46%; m.p. 86°C. IR (neat, cm^{-1}) 3535 b ν(OH), 3425 m ν(NH), 1232 s ν(P=O), 1036, 1016 s ν(P-O-Alkyl), 984, 970 s ν(CH-P). ^1H NMR (DMSO-d_6) δ (ppm): 5.03 (d, 1H, J_{HP} = 23.21), 3.93–4.23 (m, 4H), 1.29 (t, 3H), 1.25 (t, 3H). Found: C, 51.98; H, 5.92; N, 3.56%; Calcd. for $C_{17}H_{21}NO_4PCl{\cdot}2H_2O$: C, 51.46; H, 5.80; N, 3.53%.

$C_{17}H_{21}NO_4PBr$ **(3b):** Yield 68%; m.p. 112 °C. IR (neat) (ν cm^{-1}) 3535 b ν(OH), 3413 m ν(NH), 1232 s ν(P=O), 1039, 1014 s ν(P-O-Alkyl), 982 s ν(CH-P). ^1H NMR (DMSO-d_6) δ (ppm): 5.05 (d, 1H, J_{HP} = 23.06), 3.94–4.25 (m, 4H), 1.31 (t, 3H), 1.26 (t, 3H). Found: C, 46.56; H, 5.30; N, 3.25%; Calcd. for $C_{17}H_{21}NO_4PBr{\cdot}2H_2O$: C, 46.23; H, 5.21; N, 3.17%.

$C_{17}H_{21}NO_4PI$ **(3c):** Yield 43%; m.p. 78–79 °C. IR (neat, cm^{-1}) 3523 b ν(OH), 3427 m ν(NH), 1230 s ν(P=O), 1036, 1011 s ν(P-O-Alkyl), 980 s ν(CH-P). ^1H NMR (DMSO-d_6) δ (ppm): 5.09 (d, 1H, J_{HP} = 23.56), 3.97–4.27 (m, 4H), 1.32 (t, 3H), 1.28 (t, 3H). Found: C, 41.40; H, 4.71; N, 2.95%; Calcd. for $C_{17}H_{21}NO_4PI{\cdot}2H_2O$: C, 41.01; H, 5.03; N, 2.81%.

$C_{18}H_{24}NO_4P$ **(3d):** Yield 55%; m.p. 97°C. IR (neat, cm^{-1}) 3523 b ν(OH), 3429 m ν(NH), 1232 s ν(P=O), 1038, 1012 s ν(P-O-Alkyl), 984 s ν(CH-P). ^1H NMR (DMSO-d6) δ (ppm): 4.99 (d, 1H, J_{HP} = 22.74), 3.97–4.20 (m, 4H), 2.28 (t, 3H), 1.28 (t, 3H), 1.25 (t, 3H). Found: C, 57.60; H, 6.46; N, 3.96%; Calcd. for $C_{18}H_{24}NO_4P{\cdot}2H_2O$: C, 57.39; H, 6.38; N, 3.72%.

RESULTS AND DISCUSSION

The PLATON[10] drawings of the molecules with 50% probability displacement thermal ellipsoids and atomic membering schemes are shown in Fig. 1. Some of the most relevant bond distances and angles are given in Table-2.

TABLE-2
SELECTED BOND LENGTHS (Å) AND ANGLES (°) OF 3a

C1-C2	1.519 (4)	N1-C8	1.364 (4)	P1-O1	1.578 (3)
C3-O4	1.358 (4)	C13-Cl1	1.748 (3)	P1-O2	1.545 (3)
C1-N1	1.454 (4)	C1-P1	1.816 (3)	P1-O3	1.463 (2)
C18-C19	1.522 (5)	N2-C25	1.375 (4)	P2-O6	1.542 (4)
C24-O9	1.362 (4)	C30-Cl2	1.737 (4)	P2-O7	1.557 (4)
C18-N2	1.457 (4)	C18-P2	1.805 (3)	P2-O8	1.468 (3)
N1-C1-C2	114.5 (2)	C25-N2-C18	122.4 (3)	O8-P2-O6	115.9 (2)
N1-C1-P1	108.6 (2)	O3-P1-O2	115.29 (15)	O8-P2-O7	115.5 (2)
C2-C1-P1	110.0 (2)	O3-P1-O1	115.39 (17)	O6-P2-O7	101.8 (2)
N2-C18-C19	114.3 (3)	O2-P1-O1	100.0 (2)	O8-P2-C18	113.78 (16)
N2-C18-P2	109.3 (2)	O3-P1-C1	113.27 (14)	O6-P2-C18	103.6 (2)
C19-C18-P2	109.9 (2)	O2-P1-C1	108.79 (17)	O7-P2-C18	104.73 (18)
C8-N1-C1	121.6 (3)	O1-P1-C1	102.66 (15)		

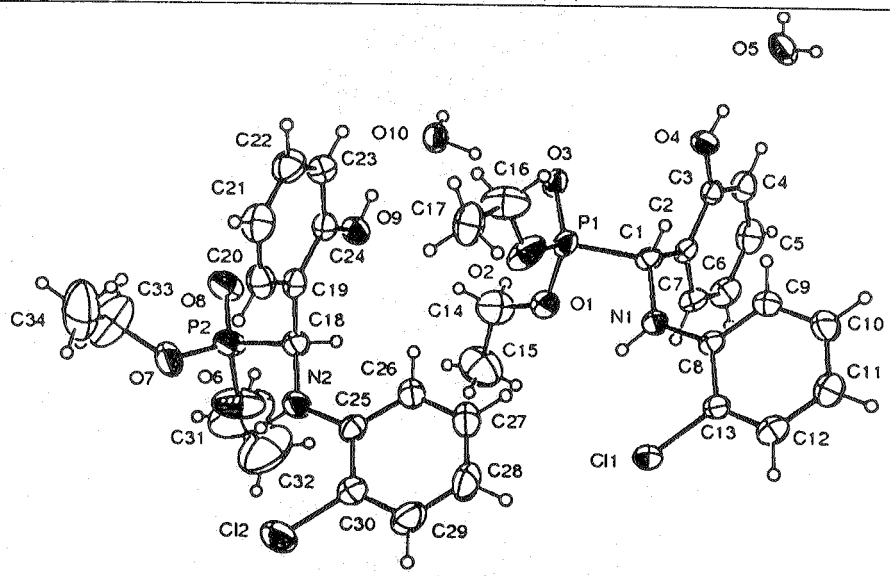

Fig. 1. PLATON drawing of the title compound **3a** with the atomic numbering schemes

IR spectra: For all compounds OH and NH stretching vibrations appear as strong bands near 3530 and 3430 cm^{-1}. The P=O stretching bands are located at 1232 cm^{-1}. The range of the P—O—Et bands is 1040–1010 cm^{-1}. C—P vibrations give rise to the bands between 985 and 970 cm^{-1}. All these assignment were made making use of literature values[3-6, 11] reported for similar structures.

^{1}H NMR spectra: The methyne proton appears as a sharp doublet and $J_{H\text{-}P}$ is in the range 22–24 Hz. Due to the asymmetric centre, the O—CH_2— and C—CH_3 groups are non-equivalent. Consequently, O—CH_2— protons appear as multiplets; C—CH_3 protons, on the other hand, give rise to two discrete triplets (no coupling to P).

X-ray Crystallography of 3a: Two independent molecules in the asymetric unit have a different conformation. The P atom has a tetrahedral environment

involving two OEt group, one asymetric C (C1) atom and one coordianted oxygen atom. The chiral centre (C1, Fig. 2) is responsible for the existence of optically active forms but in the crystal structure there are equal numbers of D and L enantiomers. Optically active forms due to an asymmetric P tetrahedron cannot be expected in this case. The P—C1 and P—O bond legths are almost comparable with similar structures[4, 6, 12]. The dihedral angles between the C2–C7 and C8–C13 phenyl ring is almost perpendicular [88.99 (12)°]. The structure is stabilized by seven intramolecular and three intermolecular hydrogen bonds (Fig. 2, Table-3).

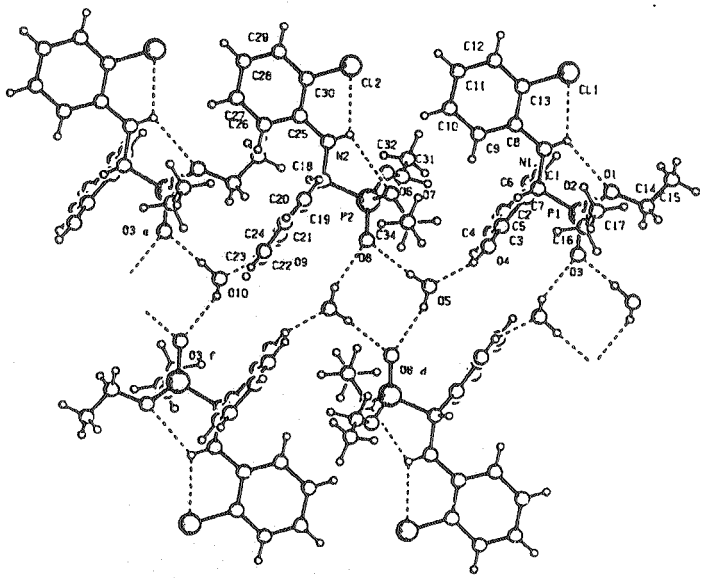

Fig. 2. Intra and Inter moleculcar hydrogen bonds network for the title compound 3a

TABLE-3
HYDROGEN-BONDING GEOMETRY (Å, °)

D-H . . . A	D-H	H . . . A	D . . . A	D-H . . . A
Intramolecular:				
N1-H1A . . . Cl1	0.8796	2.4790	2.921(3)	111.66
N1-H1A . . . O1	0.8796	2.5349	2.924(4)	107.66
N2-H2 . . . . .Cl2	0.8804	2.5036	2.940(4)	111.29
N2-H2 . . . . .O7	0.8804	2.5839	2.976(4)	108.02
O4-H4 . . . . .O5	0.8399	1.8509	2.659(4)	160.85
O9-H9 . . . . .O10	0.8399	1.8491	2.638(4)	155.92
O10-H102 . .O3	0.9213	1.8484	2.769(4)	177.97
Intermolecular:				
O5-H51 . . . .O8*	0.7879	2.0979	2.855(5)	161.29
O10-H102 . .O3*	0.8366	2.1387	2.855(4)	143.45
O5-H52 . . . .O8**	0.8323	2.0013	2.818(4)	166.88

*1 − x, −y, −z; **x, y, 1 + z

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