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Mediterranean Journal of Chemistry

Mediterranean Journal of Chemistry **2022**, 12(1), 71-82

Synthesis, X-ray structure and antibacterial evaluation of *P*-[{[bis (dimethylamino)phosphoryl]amino]} (2-chloroquinolin-3-yl) methyl]-, *P*- (quinolin-3-yl) tetramethylphosphonic diamides

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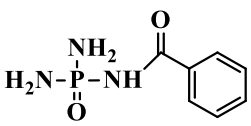
Abstract: A new *P*-bis [(dimethylamino) phosphoryl] amino} (2-chloroquinolin-3-yl) methyl]- *N*, *N*,*N*',*N*'-tetramethylphosphonic diamide was synthesized by the reaction of trisdiaminophosphine to 2-chloroquinolin-3-aldoxime. The structure of *P*-bis [(dimethylamino) phosphoryl] amino} (2-chloroquinolin-3-yl) methyl]- *N*, *N*,*N*',*N*'- tetramethylphosphonic diamide is confirmed by X-ray diffraction studies. On the other hand, the neucluphilic attack of aminophosphine on 2-chloroquinolin-3-carboimines produced different products, depending on the stability of dipolar phosphorylhexamethyl amide intermediates. Furthermore, the reaction of 3-((5-oxo-2-phenyl-oxazol-4(5H)-ylidene) methyl) quinolin-2(1H)-one with phosphine yielded alkene adduct, the Z structure is confirmed by X-ray analysis. *P*-[(2-Chloro-quinolin-3-yl)(5-hydroxy-3-methyl-1-phenyl-1*H*-pyrazol-4-yl) methyl]-*N*,*N*,*N*,*N*,tetramethyl-phosphonic diamide was obtained from reaction of 4-((2-chloro-quinolin-3-yl) methylene)-3-methyl-1- phenyl-1H-pyrazol-5(4H)- one with reagent trisdiaminophosphine. Antibacterial evaluation of most compounds exhibited moderate activity to Gram positive and Gram-negative bacteria species.

Keywords: Trisdiaminophosphine; Chloroquinolin-3-carbaldehydes; Tetremethylphosphnic diamides; X-ray crystallography; Antibacterial evaluation.

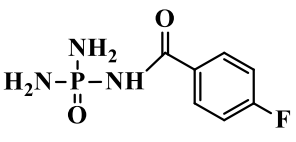
1. Introduction

Organophosphorus compounds (OPCs) are essential in agriculture, industry, biological, and pharmacy applications [1-3]. A large family of OPCs has represented an attractive approach for developing new pharmaceutical drugs [4].

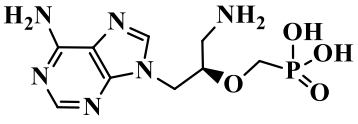
Many phosphorus-containing drugs are designed in O-P, phosphonates C-P, phosphorotriamidates, bisphosphonates P-C-P, and phosphoramides to achieve higher selectivity and bio-availability (Fig. 1). For example, phosphonate derivatives of heterocyclic bases have been shown to inhibit nucleoside phosphorylase by Tenofovir disoproxil phosphate and also inhibit nucleotide analogs reverse-transcriptase (NtRTI) for hepatitis B therapy. Remdesivir is an antiviral nucleotide analog, recently authorized for emergency use as a drug against COVID-19. At the same time, sofosbuvir is a nucleotide analog inhibitor of NS5B polymerase developed for hepatitis C therapy (Fig) [5-7]. Chloroquine phosphate is an autophagy and toll-like receptors (TLRs) inhibitor and is highly effective in controlling SARS-CoV-2 (COVID-19) infection in vitro. Also, pyridyl-base derivatives exhibit antioxidant, antiviral, and antimicrobial activity [8,9].



Tolfamide



Flurofamide



(S)-HPMPA(Antiviral drug)

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DOI: http://dx.doi.org/10.13171/mjc02206211632arsanious

Received May 16, 2022
Accepted June 6, 2022
Published June 21, 2022

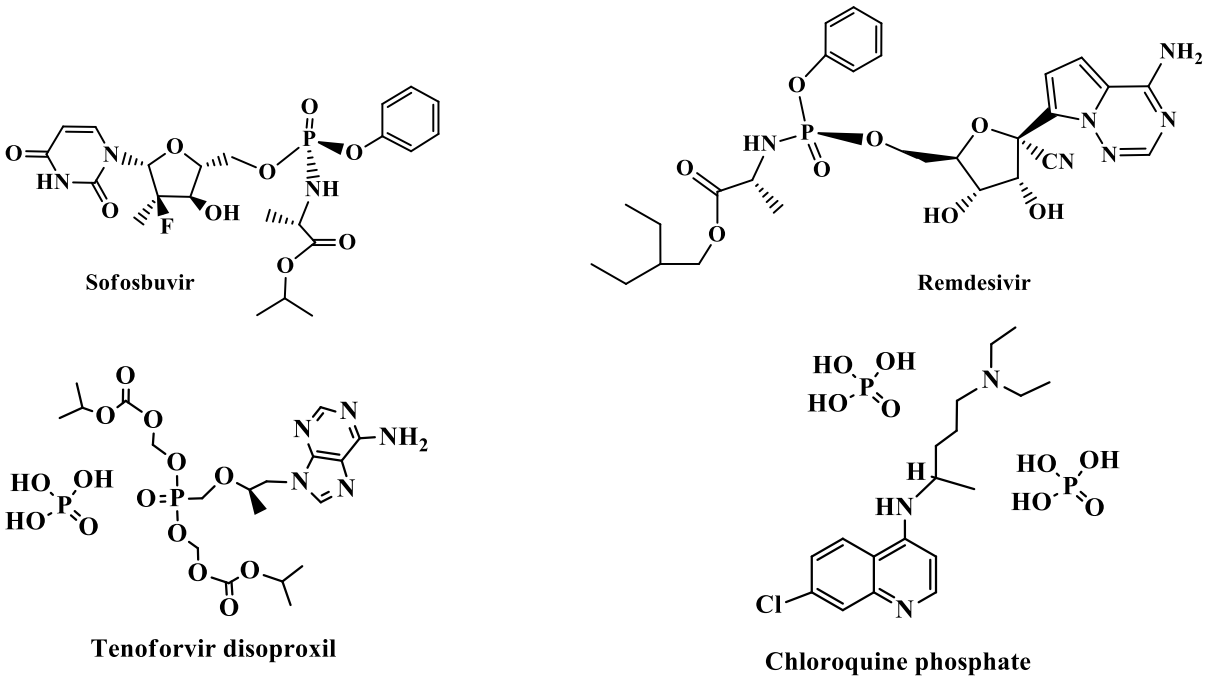


Figure 1. Structures of phosphorotriamidate phosphonate and α-aminophosphonic acid derivatives

The present study deals with the synthesis of quinoline derivatives bearing functional phosphorus residues. In order to implement this goal, the reactions of 2-chloroquinoline-3-carbaldehyde derivatives **2a-d**, **7**, and **9** with tris(di-methylamino) phosphine **1** have been investigated. X-ray crystallography studies were reported for new products **3** and **8**. Moreover, their antibacterial activities were evaluated (Fig. 2).

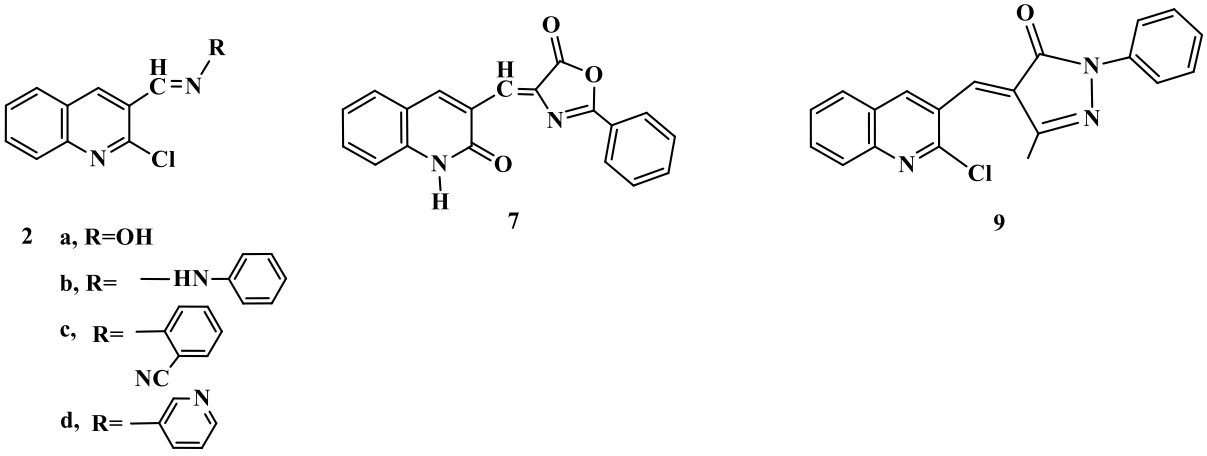


Figure 2. Starting materials

2. Results and Discussion

P-{Bis[(dimethylamino)phosphoryl]amino}(2-chloroquinolin-3-yl)methyl]N,N,N',N'-tetramethyl phosphonic diamide compound **3** was obtained through reaction of trisdiaminophosphine **1** with 2-chloroquinolin-3-aldoxime **2a** in 10 cm^3 of DMF and heating in an oil bath at 108˚C for 2hrs. ^{1}H NMR spectrum of **3** exhibited two doublets at δ 2.12, 2.61ppm for [P-(N(CH$_3$)$_2$)$_2$]$_2$, 24H, J_{HP} = 8.60 Hz) and doublet of a doublet at δ 5.47 (J_{Hp}= 15.68 Hz, $^2J_{HP}$= 7.48 Hz) due to P-CH-N-P proton [10]. On the other hand ^{13}C NMR spectrum showed NMe_2 at δ = 36.8, whereas P-CH-N-P at δ = 49.4 (P-C-N-P, $^1J_{CP}$ = 96Hz, $^2J_{CP}$ = 38Hz). Moreover, the assigned structure of compound **3** was unambiguously supported by X-ray analysis (Fig. 3).

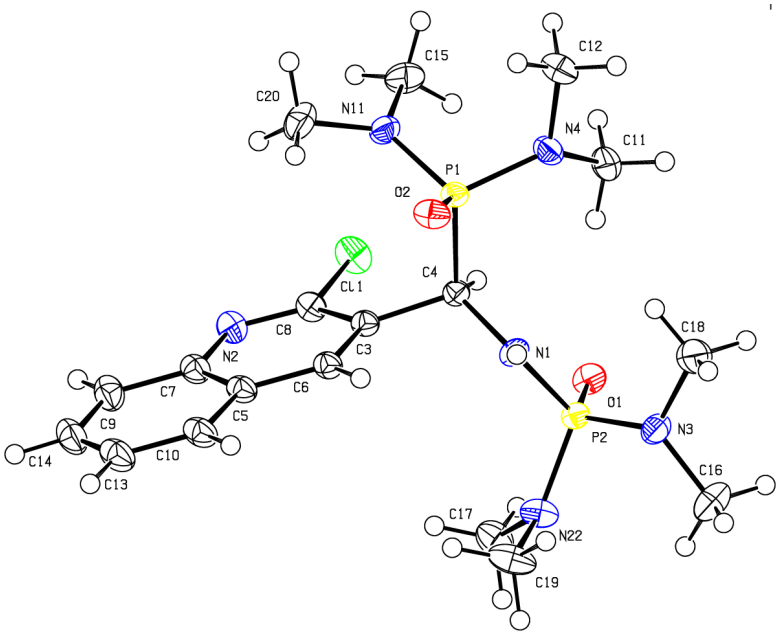
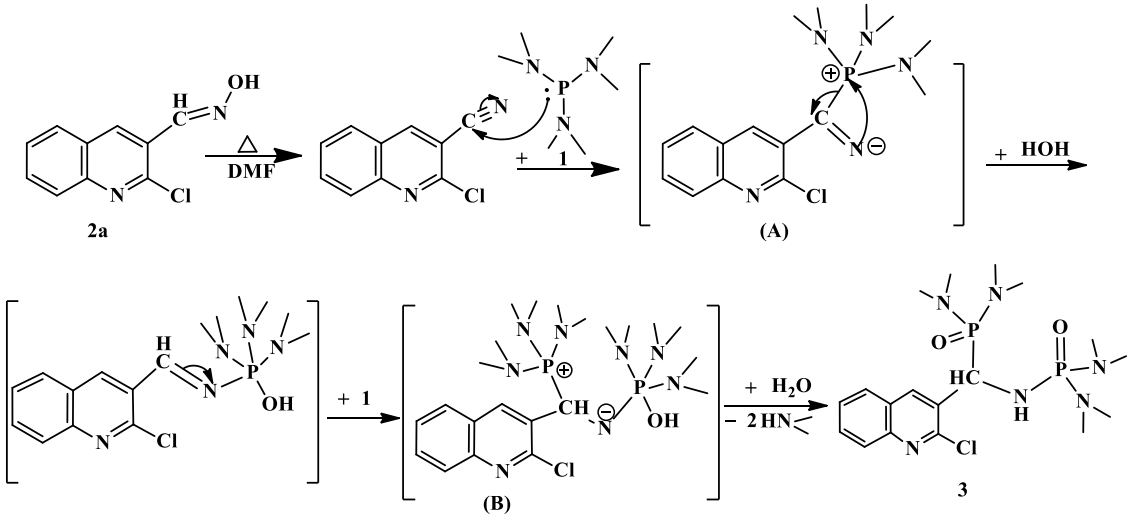


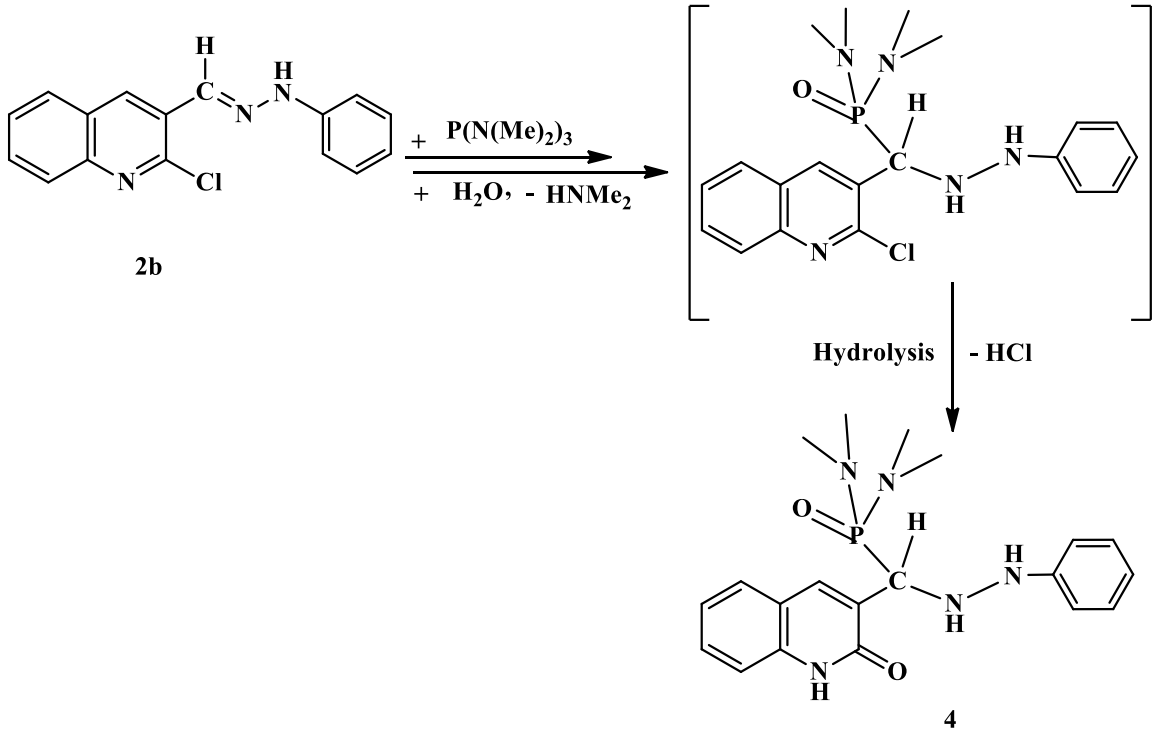
Figure 3. ORTEP diagram of compound **3**

The formation of compound **3** is outlined in Scheme 1. Initially, the reaction involved dehydration of –CH=N-OH group in **2a,** followed by nucleophilic attack of one molecule phosphine **1** on the produced nitrile to generate the dipolar intermediate (**A**). Molecular rearrangement of (A), followed by the addition of one molecule of water and attack of another molecule of phosphine **1** to imine group HC=N-P, led to the formation of intermediate (B). Finally, the sequence of addition of the element of water and ejection of two moles of $HN(CH_3)_2$, resulted in the formation of compound **3** [11,12].



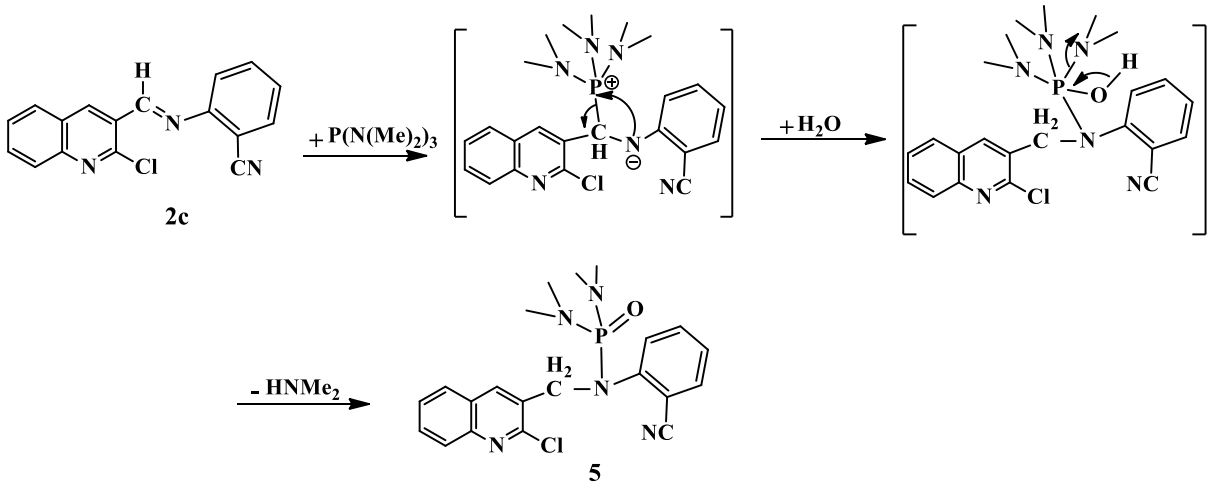
Scheme 1. Formation of compound 3

N,N,N',N'-tetramethyl-P-[(2-oxo-1,2-dihydro quinolin-3-yl) (2-phenylhydrazinyl) methyl] phosphonic diamide 4 was obtained from the reaction of 1-((2- chloroquinolin-3yl) (methylene))-2-phenyl-hydrazine 2b with the amino-phosphine reagent 1 in refluxing toluene. The structure of compound 4 is based on ^{1}H-, ^{13}C-NMR, and mass spectral data. The formation of compound 4 is outlined in Scheme 2 [1]



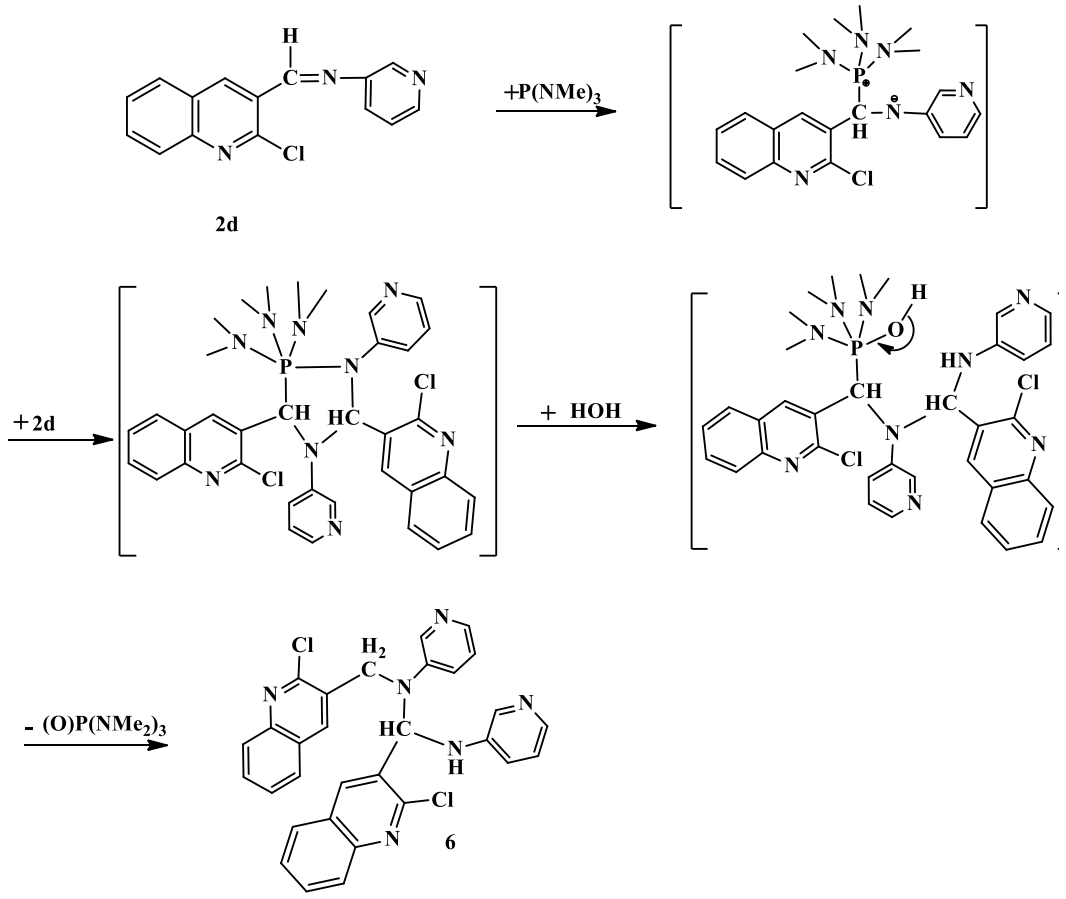
Scheme 2. Formation of compound 4

On the other hand, the reaction of trisaminophosphine **1** with 2-chloroquinoline-3-imine **2c** yielded phosphorylated adduct **5.** The assigned structure **5** was based on the ^{1}H-, ^{13}C-NMR, and mass spectral data. The ^{1}H-NMR spectrum of **5** exhibited two doublets that appeared at 2.25, 2.71(12H, $^{3}J_{HP}$ = 10.4 Hz) due to protons of the two N, N-dimethylamino groups. Methylene protons appeared as two dd which are centered δ = 4.67, 4.65 (J_{HH} = 12.40 Hz, J_{HP} = 8.80 Hz), and δ = 4.75, 4.70 (J_{HH} = 12.80 Hz, J_{HP} =8.80 Hz). The ^{13}C-NMR spectrum of compound **5** showed signals at 36.3 corresponding to $N(CH_3)_2$ and 52.6 due to CH_2, $^{2}J_{CP}$ = 30.0 Hz. The formation of **5** is explained in Scheme 3.



Scheme 3. Formation of compound 5

Treatment of compound **2d** with trisdimethylaminophosphine **1**, led to the formation of compound **6**. The structure of compound **6** was established based on its spectral data (^{1}H-, ^{13}C-NMR, MS, IR). The formation of compound **6** is explained in Scheme 4.



Scheme 4. Formation of compound 6

[(Z)-3-(Dimethylamino)-3-oxo-1-(2-oxo-1,2-dihydro quinolin-3-yl) propenyl] benzamide **8** is derived from the reaction of 3-(5-oxo-2-phenyl-oxazol-4(5H)-quinolin-2(1H)-one **7** with aminophosphine **1**, using DMF as solvent. The X-ray crystallographic analysis confirmed the existence of compound **8** in Z-structure (Fig. 4, Table 1).

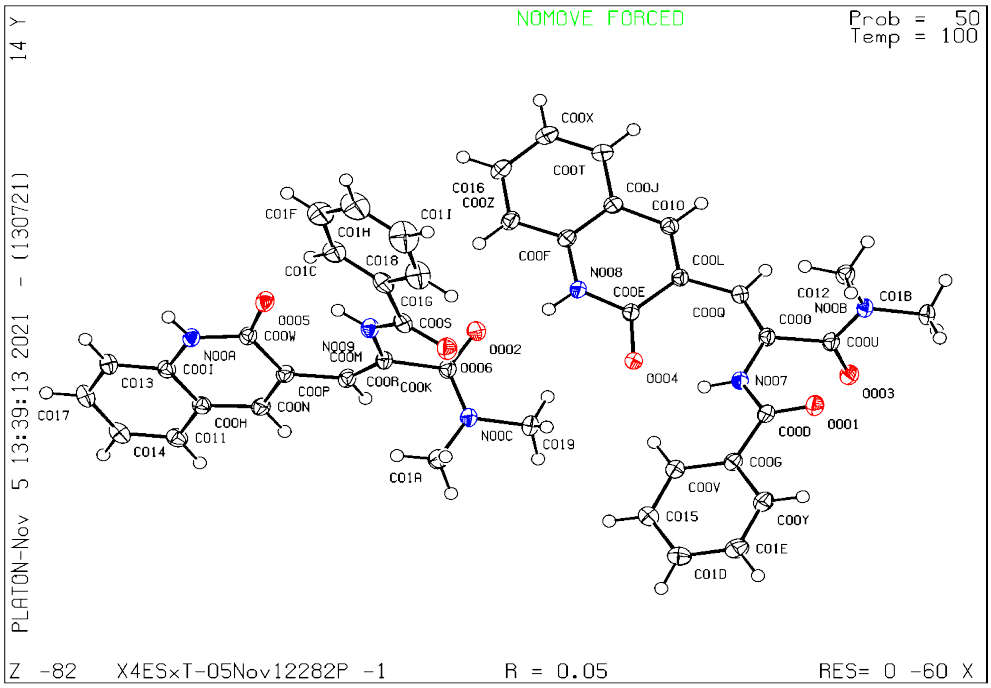
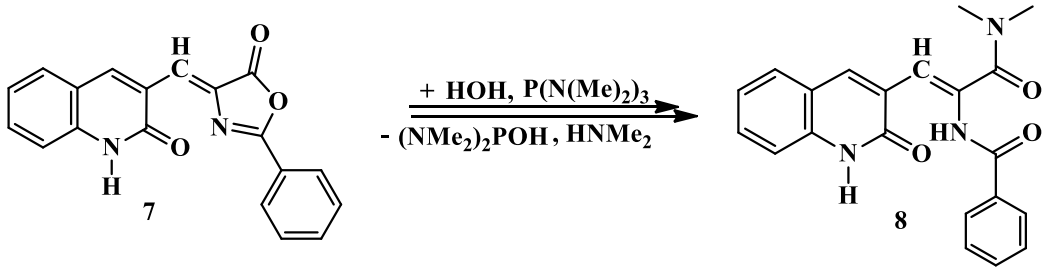


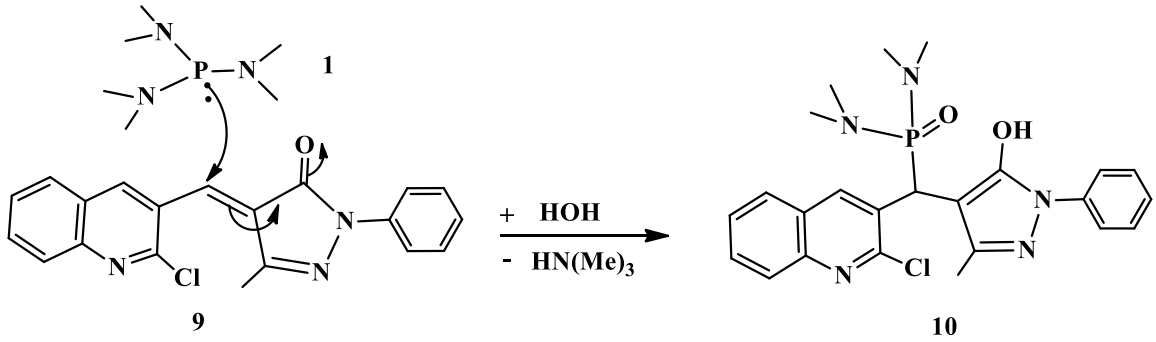
Figure 4. ORTEP diagram of compound **8**

The formation of compound **8** is outlined in Scheme 5. The initial step involved hydrolysis of lactone function followed by the attack of the phosphine **1** to β-unsaturated carboxylic group to produce 3-[(dimethylamino)-3-oxo-1-(2-oxo-1,2-dihydro-quinolin-3-yl) propenyl] benzamide **8** Scheme 5 [13].



Scheme 5. Formation of compound 8

4-((2-chloroquinolin-3-yl)methylene)-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one **9** reacted with aminophosphine **1** to give compound **10**. ^{1}H-, ^{13}C-NMR, mass, and IR spectral data confirmed the structure of **10**. The formation of compound **10** is outlined in Scheme 6.



Scheme 6. Formation of compound 10

2.1. Crystallographic analysis

2.1.2. X-ray Crystal structure determination

Intensity data of X-ray crystals **3**,**8** were collected at 100(2) K at the XRD1 beam line of the Electra Synchrotron, Trieste (Italy) [14], using a monochromatic wavelength of 0.700 Å on a Pilatus 2M hybrid-pixel area detector (DECTRIS Ltd, Baden-Daettwil, Switzerland) Table 1. CCDC 2086490 for compound **3**; CCDC number: 2171880 for compound **8** contains the supplementary crystallographic data. These data can be obtained free of charge via https://www.ccdc.cam.ac.uk/structures/, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033, or e-mail: HYPERLINK"mailto: deposit@ccdc.cam. ac.uk "deposit@ccdc.cam.ac.uk.

The crystals of compound **3** were dipped in NHV oil (Jena Bioscience, Jena, Germany) and mounted on the goniometry head with nylon loops. During data collection, no crystal decay was observed. Data reductions were performed with XDS [15]. All the structures were solved with SHELXT [16] and refined with SHELXL-2018/3 implemented in WinGX – Version 2014.1 system. The program Mercury [17] was used for graphics. Thermal motions for all nonhydrogen atoms were treated anisotropically, and hydrogens were included in calculated positions, riding on their carrier atoms. Hydrogen atoms were included at calculated positions with isotropic $U_{factors}$ = 1.2×U_{eq} or $U_{factors}$ = 1.5×U_{eq} for methyl groups (U_{eq} being the equivalent isotropic thermal factor of the bonded nonhydrogen atom).

Compound **3** crystallizes in the orthorhombic space group *Pbca* with eight molecules in the unit cell, i.e. one molecule per asymmetric unit cell. Fig. 3 illustrates the ORTEP diagram of 3.

Considering that the compound crystallized in a centrosymmetric space group, the structure is racemic despite the asymmetric unit containing only an enantiomer. While the angles C3-C4-P1 (106.24(8)), C3-C4-N1(114.61 (10)), and P1-C4-N1 (108.76(8)) have values close to 109.5°, the angle formed by P2-N1-C4 (121.94(8)) is close to 120°, indicating a resonance involving the P2-N1 and the P2-O1 bonds (Fig. 3).

Generally, this compound's bond lengths and angles (Table S3) are comparable to the solved structure by [18], and others have similar construction [19-24]. A view of the packing diagram (Fig. 5) shows that the crystal structure of **3** is stabilized through two strong intermolecular hydrogen bonds N(1)—H…O(2) (Fig. 5 and Table 2), allowing the formation of dimmers [25-26]. In addition, other weaker hydrogen

bonds are observed between methyl groups and nitrogen and oxygen atoms within the same molecule (Table 2) [14-20]. The 2-chloroquinoline group is predominantly planar, and the plane that contains the two phosphorus atoms and carbon C4 atom is nearly perpendicular to that of 2-chloroquinoline with a dihedral angle of 89.1° (Fig. 6). The P-O bonds point in opposite directions concerning the plane P2-C4-P1.

Table 1. Crystallographic data for compounds **3** and **8**.

	3	8
Crystal Data		
Moiety formula	$C_{18}H_{31}ClN_6O_2P_2$	$C_{21}H_{19}N_3O_3$
M / Da	460.88	361.39
Crystal system	Orthorhombic	triclinic
Space group	*P b c a* (n. 61)	*P*-1
a / Å	15.107(3)	11.032(2)
b / Å	15.246(3)	12.494(3)
c / Å	19.684(4)	13.818(3)
α / °	90	86.16(3)
β / °	90	79.40(3)
γ / °	90	76.06(3)
V / Å^3, *Z*	4533.6(16), 8	1816.5(7)
Temperature / K	100(2)	100(2)
Reflns for cell det	12498	12498
θ / ° for cell det	0.98-29.98	0.98-29.98
D_x / Mg m^{-3}	1.35	1.321
Colour, habit	Light yellow, plates	Light yellow, plates
Data Collection		
Temperature / K	100(2)	100(2)
radiation λ / Å	synchrotron, 0.700	synchrotron, 0.700
Scan type	φ	
$2\theta_{max}$ / º	59.96	59.96
h range	–21 → 21	-15→15
k range	–21 → 20	-17→17
l range	–23 → 28	-19→19
Measured reflns	6892	10522
Reflns with $I>2\sigma(I)$	5797	9885
R_{int}	0.0368	0.0465
Refinement on F^2		
R_1, wR_2 [$F^2>2\sigma(F^2)$]	0.0389, 0.1066	0.0465,0.1304
R_1, wR_2 [all data]	0.0452, 0.1125	0.0482,0.1323
S	1.037	1.037
Params, restraints	270, 0	491.0
$(\Delta/\sigma)_{max}$	0.001	0.001

Table 2. Inter- and intra-molecular hydrogen bonds for compound **3**.

Type	D—H···A	D—H	H···A	D···A(Å)	D—H···A(˚)
Inter	N(1)—H(1)···O(2)i	0.88	2.08	2.869(1)	148.9
	C(4)—H(4)···O(1)	1.00	2.46	2.974(1)	111.1
Intra	C(16)—H(16B)···N(22)	0.98	2.43	2.944(2)	112.3
	C(17)—H(17B)···O(1)	0.98	2.45	2.934(2)	110.2
	C(18)—H(18B)···N(1)	0.98	2.45	2.958(2)	111.5
	C(20)—H(20B)···O(2)	0.98	2.46	2.969(2)	112.0

Symmetry codes: (i) -x+1, -y+1, -z+1

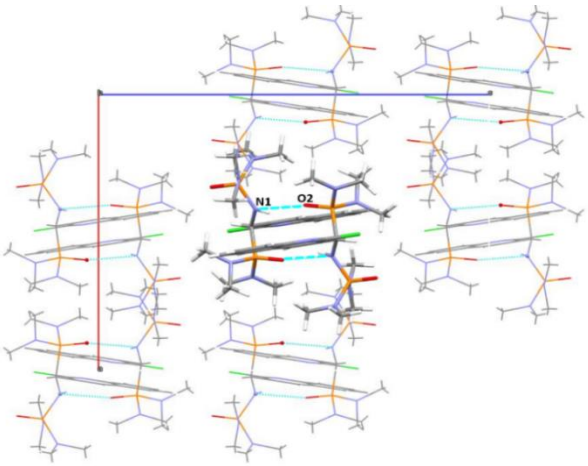


Figure 5. Packing diagram 3 shows the intermolecular hydrogen bonding along with the b axis (a) and rotated by 50 degrees along the b axis (b)

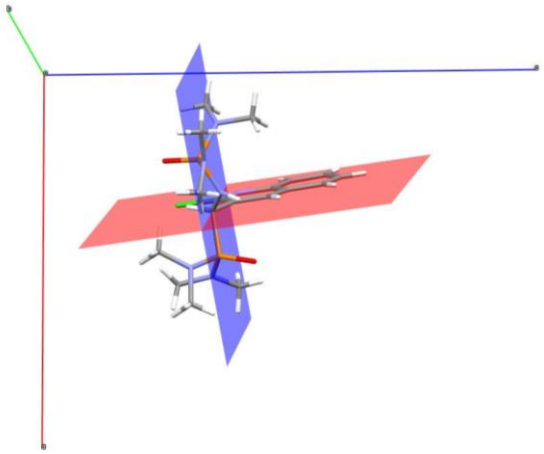


Figure 6. Average planes across the two phosphorus atoms, the carbon C4 atom (blue), and the carbon atoms of the 2-chloroquinoline group (red). The dihedral angle is 89.1°

2.2. Biology study

Compounds **2a-2c**, **3-5,** and **9,10** were tested for their antibacterial activity against Gram-negative (*Escherichia coli* and *Pseudomonas aeruginosa*) and Gram-positive (*Bacillussubtilis, Staphylococcus aureus,* and *Bacillus cereus*), using the diffusion plate method. The MIC(µg /ml or 100%), values were determined for each of the pathogens. The zone of inhibition was measured in mm and recorded. Ampicillin and Kanamycin at µg/ml or 100%) were used as standards in the experiment [27,28]. The antibacterial evaluation of the new compounds, *P*-bis[(di-methylamino) phosphoryl] tetramethyl phosphonic diamide compound **3** was shown to be the most active agent against Gram-positive and Gram-negative bacteria compared to the other tested compounds (Table 3). Compound **4** and compound **10**, exhibited more activity against Gram-positive (*Bacillus Cereus*) [29]. It was noted that compound **8** had no antibacterial activity.

Table 3. Antibacterial properties of compounds **2a-c, 3-5,** and **8-10**.

Sample		Inhibition zone diameter (mm/mg Sample)				
		Gram-positive bacteria			**Gram-negative bacteria**	
		Bacillus subtilis	*Staphylococcus aureus*	*Bacillus Cereus*	*Escherichia Coli*	***Pseudomonas aeruginosa***
Stander	Ampicillin	26	21	0.0	25	26
	Kanamycin	0.0	26	25	0.0	0.0
Compound 2a		0.0	0.0	0.0	0.0	0.0
Compound 3		13	15	0.0	15	16
Compound 2b		0.0	0.0	0.0	0.0	0.0
Compound 4		0.0	15	14	14	13
Compound 2c		0.0	14	0.0	12	11
Compound 5		12	14	0.0	12	11
Compound 8		0.0	0.0	0.0	0.0	0.0
Compound 9		0.0	10	10	11	10
Compound 10		0.0	14	15	12	12

Disc diameter 5mm; Control DMSO

3. Conclusion

We synthesized new derivatives of 2-chloroquinolin-3-carbaldehydes bearing imines group and heterocyclic rings in this work. Introducing one or two groups of $O=P(NCH3)_2$, using diaminhosphine as a reagent, may increase the biological activity. The reaction of trisaminophosphine and 2-chloro-quinolin-3-aldoxime led to the formation of, *P*-bis (dimethylamino) phosphoryl] amino} (2-chloro-quinolin-3-yl-)methyl]-*N*,*N*,*N*',*N*'-tetra-methyl phosphonic diamide. Due to its particular design, it represents a new promising agent. X-Ray studies were essential to conform the suggested structure of *P*-bis(dimethylamino) phosphoryl] amino} (2-chloroquinolin-3-yl-) methyl] phosphonic diamide. Also, the reactions of 2-chloroquinolin-3-carbaldehydeimines with trisaminophosphine led to the formation of phosphorylphenylhydrazine, 2-cyanoanilinophosphorylamidate, and *N*-[(2-chloro-quinolin-3-yl) *N*,*N*'-di(pyridin-3-yl) methane diamine. Furthermore, 3-(5-oxo-2-phenyl-oxazol-4(5H)- quinolin-2(1H)-one reacted with phosphine reagent to produce N-[(Z)-3-(dimethylamino)-3-oxo-1-(2-oxo-1,2-dihydro-quinolin-3-yl) prop-1-en- 2-yl]benzamide**.** The assigned Z structure is based on X-ray analysis. P-[(2-Chloroquino-lin-3-yl) (5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl) methyl] tetramethylphosphonic diamide is generated by the reaction of aminophosphine with 2-chloroquinolyl-3-methyl-1-phenyl-1H-pyrazol-5(4H)-one. The stability of dipolar intermediates in the reactions of aminophosphine plays an important role in the formation of new products.

From the antibacterial evaluation, it could be concluded that *P*- bis[(dimethylamino) phosphoryl] tetramethylphosphonic diamide is the most active against gram-positive and gram-negative bacteria compared to other compounds. P-[(2-oxo-1,2-dihydroquinolin-3-yl)(2-phenylhydrazinyl) methyl]-, and P-[(2-chloroquinolin-3-yl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl) methyl]- phosphonic diamides , exhibited moderate activity against Gram-+ve (*Bacillus Cereus*) specie.

4. Experimental Section

4.1. General remarks

Chemicals were purchased from Aldrich Chemical Co. and used as such without further purification. Completion of the reaction was indicated by thin-layer chromatography. The IR spectra were measured with a Bruker spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on Jeol and Bruker spectrometers (400, 500, and 100,125 MHz, respectively) in $CDCl_3$ and C_5D_5N.

4.2. Synthetic procedure

To a solution of **2a-d, 7,** and **9** (1 mmol) in 10 cm^3 DMF/ or toluene, trisdimethyl aminophosphine **1** (2 mmol) was added dropwise at room temperature with stirring, and the reaction mixture was heating in an oil bath at 108°C for 2-4hrs. The reaction mixture was evaporated under reduced pressure, and the residue was applied to silica-gel column chromatography. The eluent solution (v:v) adducts **3-6**, **8,** and **10** were separated.

***P*-{Bis (dimethylamino) phosphoryl] amino} (2-chloroquinolin-3-yl) methyl]- *N,N,N',N'*-tetramethylphosphonic diamide 3.**

eluent; ethyl acetate: methanol (98:5; v: v); compound **3** was obtained as crystals; 0.31 g (67%); m..p 237-238°C;

IR: V_{max}/cm^{-1} : (NH) 3104, (P=O) 1258, [P[(N- $(Me)_2$) $]_2$] 1335, 838;

^{1}H NMR (C_5D_5N) *d*/ppm: 2.12 (d, 6H, $^3J_{PH}$ = 9.5 Hz, NMe_2, H-3), 2.19(d, 6H, $^3J_{PH}$ = 8.64 Hz, NMe_2), 2.61 (d, 6H, $^3J_{PH}$ = 8.6 Hz, NMe_2), 2.83 (d, 6H, $^3J_{PH}$ = 8.44 Hz, NMe_2), 5.43-5.49 (2d, 1H, J_{Hp} = 15.68 Hz, $^2J_{HP}$ = 7.48 Hz, CH) ,7.58 (t, 1H, *J* = 7.64 Hz, ArH), 7.75 (t, 1H, *J* = 7.08 Hz, ArH), 8.89 (d, 1H, *J* = 15.02 Hz), 7.97(d, 1H, *J* = 8.60 Hz, ArH), 8.55 (s, 1H, ArH);

^{13}C NMR (C_5D_5N) *d*/ppm: 36.34 (NMe_2), 49.45(P-C-N-P, J_{CP} = 96Hz, $^2J_{CP}$ = 38Hz), 128.7,128.0, 128.6, 130.7, 131.9 , 134.2,137.8, 141.4, 145.0, 151.6 (C-Ar);

MS *m/z* : 460 (M^+, 5%);

Anal. Calcd. Mass fractions of elements, w / % for $C_{18}H_{31}ClN_6O_2P_2$ (M_r = 460.16) are: C 46.91, H 6.78, Cl7.69, N18.23,P13.44; found: C 46.62, H 6.53, Cl 7.60, N 18.18,P 13.40.

***N,N,N',N'*-tetramethyl-P-[(2-oxo-1,2-dihydroquinolin-3-yl)(2-phenylhydrazinyl) methyl]phosphonic diamide 4.**

eluent; acetone: petroleum ether (30:70; v: v); compound **4** was obtained as crystals; 0.24 g (60%) m.p: 197-198°C;

IR: V_{max}/cm^{-1}: (NH) 3348, 3055, 2921, (P=O) 1258 [P[(N $(Me)_2$)]$_2$] 1325, 886;

^{1}H NMR ($CDCl_3$) *d*/ppm: 2.82 (d, 6H, ^3J= 10.0 Hz, NMe_2, P-H), 3.02(d, 6H, J_3= 10.0 Hz, NMe_2), 4.99-4.95 (d, 1H, J_2 = 14.0 Hz, CH),6.60 (d, 2H, *J* = 10.0 Hz, ArH), 6.73 (d, 2H, *J* = 10.0 Hz, ArH), 7.11(d, 2H, *J* = 7.60 Hz, ArH), 7.24(s,1H, ArH), 7.67(m,1H, ArH), 8.49(s, 1H, ArH), 9.56 (s, 2H, 2NH), 9.72(s, 1H, NH);

^{13}CNMR($CDCl_3$) *d*/ppm: 36.3 (NMe_2), 50.0(d, J_{CP} = 62.0 Hz, C-P), 113.3, 120.5, 125.1,128.4, 129.1, 130.6, 133.0, 137.5, 144.7, 147.7 (C-Ar);

MS *m/z* : 400 (M^++1, 5%),

Anal. Calcd. Mass fractions of elements, w / % for $C_{20}H_{26}N_5O_2P$ (M_r=399.42) are: C60.14, H6.56, N17.53,P7.75; found: C60.20, H6.46, N 17.42 , P7.71.

P-[(2-chloroquinolin-3-yl)(2-cyanoanilino) methyl]-N,N,N',N'-tetramethylphosphonic diamide 5.

eluent; acetone: methanol (98:5; v: v); compound **5** was obtained as crystals; 0.23 g (55%) m.p: 242-243°C;

IR: V_{max}/cm^{-1}: (NH) 2165,(P=O)1233, P[(N-$(Me)_2$)]$_2$1335, 850 ;

^{1}H NMR ($CDCl_3$) *d*/ppm 2.25 (d, 6H, *J* = 11.6 Hz, $PNMe_2$), 2.71(d, 6H, ^3J= 10.0 Hz, $PNMe_2$), 4.67, 4.62 (dd, 1H, J_{HH} = 12.40,J_{PH} = 8.80 Hz, CH_2-phosphamidate), 4.75, 4.70 (dd, 1H, J_{HH} = 12.80, J_{PH} = 8.80 Hz, CH_2 phosphamidate), 6.75 (d, 2H, *J* = 9.20 Hz, Ar-H),7.31 (d, 2H, *J* = 8.80 Hz, Ar-H),7.67 (t, 1H, *J* = 11.60 Hz, Ar-H), 7.81 (t, 1H, *J* = 8.40 Hz), 8.16-8.12 (m,2H,Ar-H);

^{13}C NMR ($CDCl_3$) *d*/ppm: 36.1, 52.6 (d, ^2J = 30.0Hz, C-N-P), 115.3, 120.5,122.8,124.5, 125.1, 126.1, 128.4, 129.1, 130.6, 132.6, 137.2, 141.4, 144.3, 150.9, 151.6;

MS *m/z* : 427 (M^+, 100);

Anal. Calcd Mass fractions of elements, w / % for $C_{21}H_{23}ClN_5OP$(M_r = 427.86): C 58.95, H 5.42, Cl 8.29,N 16.37,P 7.24; found: C 58.78, H 5.30, Cl 8.15,N 16.30,P 7.20.

1-(2-chloroquinolin-3-yl)-N-[(2-chloroquinolin-3-yl)methyl]-N,N'-di(pyridin-3-yl)methanediamine 6.

eluent; ethyl acetate: petroleum ether (60:40; v: v); compound **6** was obtained as crystals; 0.31 g (70%) m.p: 245-246°C;

IR: V_{max}/cm^{-1} : (NH) 3055;

^{1}H NMR ($CDCl_3$) *d*/ppm 4.26 (s,2H,CH_2), 4.85 (s,1H,CH),4.94(s,1H,NH), 7.49-7.44(m, 3H, ArH), 7.69 -7.67(m, 4H, ArH), 7.69-7.67(d,2H, *J*= 8.0Hz, ArH),7.89-7.85 (m,4H, ArH), 8.04-8.01 (m, 3H, ArH),8.23(s, 2H, ArH);

^{13}C NMR ($CDCl_3$) *d*/ppm: 58.5(CH_2), 59.8(CH), 125.6, 126.0, 127.2, 127.3, 128.2, 134.6, 136.7, 147.0,147.8, 149.1, 162.7.

MS *m/z* : 535 (M^+-1, 40%).

Anal. Calcd. Mass fractions of elements, w / % for $C_{30}H_{22}Cl_2N_6$ (M_r = 536.15) are: C 67.04, H 4.13, Cl 13.19,N 16.64; Found: C 67.12, H 4.06, Cl 13.22 , N 16.58.

N-[(Z)-3-(dimethylamino)-3-oxo-1-(2-oxo-1,2-dihydroquinolin-3-yl)prop-1-en-2-yl]benzamide 8.

eluent; ethylacetae : petroleum ether (80:20; v : v); compound **8** was obtained as crystals; m.p 280-281˚C.;

^{1}H NMR (C_5D_5N) *d* / ppm: 3.13, 3.09 (2s, 6H, NMe_2), 4.91(s, 1H, =CH), 7.18(s, 1H, ArH), 7.20-7.24 (m, 1H, ArH), 7.40 -7.46 (m, 3H, Ar-H), 7.48-7.55 (m, 2H, ArH),7.63 (d, 1H, *J*= 8.0Hz, Ar H), 8.24 (d, 2H, *J* = 15.02 Hz), 13.72, 13.58(2s, 2H, 2NH);

^{13}C NMR (C_5D_5N) *d* / ppm: 34.7 (NMe_2), 110.4, 115.3, 120.6, 122.8, 123.5, 128.0, 128.6, 130.7,132.3, 134.5, 135.3, 138.2, 141.4, (C-Ar), 162.8, 163.4, 168.8 (C =O);

MS *m/z* : 361 (M^+, 20%).

Anal. Calcd Mass fractions of elements for $C_{30}H_{22}Cl_2N_6$(Mr =361.14) are: C7.04, H 4.13, Cl 13.19, N 16.64; found: C 7.12, H 4.06, Cl 13.22, N16.58.

P-[(2-chloroquinolin-3-yl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl) methyl]-N,N,N',N'-tetramethyl-phosphonic diamide 10.

eluent; acetone: petroleum ether (60:40; v: v); compound **10** was obtained as crystals; 0.22 g (45%) m.p : 234-235°C;

IR: V_{max}/cm^{-1} : (OH) 2973, (P=O)1258, [P[(N-$(Me)_2$)]$_2$] 1345, 817;

^{1}H NMR ($CDCl_3$) *d*/ppm: 1.65(s, 3H, CH_3), 2.37

(d, 6H, $J_{1,3}$ = 9.20 Hz, NMe_2, H-3), 2.83(d, 6H, $J_{1,3}$ = 9.20 Hz, Me_2), 3.79 (d, 1H, $J_{1,2}$ = 14.5 Hz, CH,H-2), 7.48-7.30(m, 4H, ArH), 7.53,7.55 (2d, 4H, *J*= 8.40 Hz, ArH), 7.95 (d, 2H, *J*= 8.40 Hz, ArH), 9.68 (1s, 1H, OH);
^{13}C NMR ($CDCl_3$) *d*/ppm: 14.8(CH_3), 36.3 (d, $J_{1,2}$ = 37.5 Hz, NMe_2, C-2), 49.0 (d, J_1 = 73.75 Hz, C-1), 119.5, 121.8, 123.5,123.8, 124.8, 126.4, 127.5, 127.7, 129.0,134.6, 136.2, 145.7, 158.7 (C-Ar);
MS *m*/*z* : 483 (M^+, 22%).
Anal. Calcd. Mass fractions of elements, w / % for $C_{24}H_{27}ClN_5O_2P$ (M_r = 483.15) are: C59.57, H5.62, Cl 7.33, N14.47, P 6.40; found: C 59. 40, H 5.57, Cl 7.30,N 14.41, P 6.36.

Acknowledgments

The authors thank XRD1 staff at Elettra Synchrotron for the in-house measurements.

Funding

The National Research Centre, Egypt, supported this work.

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