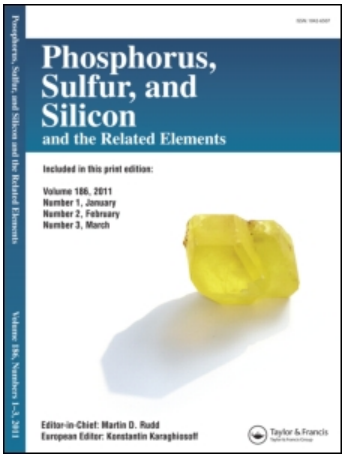

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Arvind K. Gupta[a]; D. K. Dubey[a]; B. D. Parashar[a]; M. P. Kaushik[a]
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An efficient synthesis of O,O- Di Propyl (E)-2-[1-methyl 2-oxopropylidene]phosphorohydrazidothiolate (E) Oxime and Its Analogues: A Potential Marine Toxin

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An efficient method for the synthesis of Ptychodiscus brevis toxin O,O- di n-propyl (E)-2-[1-methyl 2-oxopropylidene]phosphorohydrazidothiolate (E) oxime (TG-1) and its analogues has been developed using thermally stable and recyclable silica gel and Na_2SO_4 as a condensing agent and water scavenger, respectively. The compounds were evaluated against fish Rasbora daniconius by determining the LC_{50} and LC_{90} values. The results of biological evaluation showed that these compounds have high degree of toxicity.

Keywords Fish toxin; phosphoric acid hydrazides; ptychodiscus brevis; thiophosphoric acid hydrazide

INTRODUCTION

Ptychodiscus brevis (*Gymnodinium breve)* is a marine *dinoflagellate,* which is the cause of massive fish kills, mollusk poisoning, and human food poisoning along the Florida coast and in the Gulf of Mexico. This class of marine toxins have attracted the attention of organic chemists due to their involvement in human intoxication and socioeconomic impact brought by those incidents.[1] Several attempts have been made to isolate the toxins from the cultured cells; however, discrepancies exist in the reported physical properties.[1–5] Presumably, the main reason is the difficulty associated with the separation and purification of the toxin mixture. Elucidation of the chemical formula is imperative not only for the understanding the molecular basis of mechanism of action but for the design of proper defensive countermeasures such

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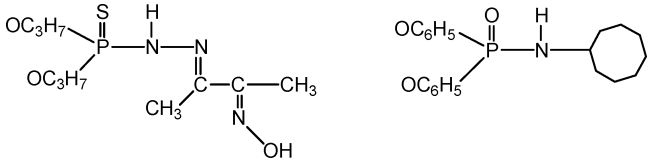


TG-1 PB-1

FIGURE 1 O,O-Dipropyl(E)-2-[1-methyl 2-oxopropylidene] phosphorohydrazidothiolate(E)oxime (TG-1) and O,O-Diphenyl N-cyclooctylphosphoramidate (PB-1).

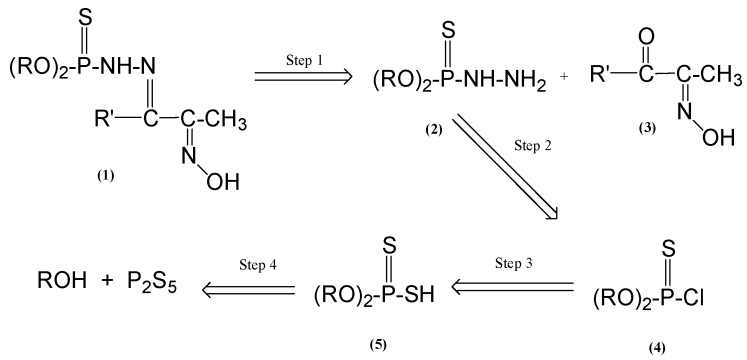
as detection, protection, and decontamination methods, as well.[6] Over the past decade, phosphorus-containing G*ymnodinium breve* toxins, such as O,O- di n-propyl (E)-2-[1-methyl 2-oxopropylidene] phosphorohydrazidothiolate (E) oxime[7] (TG-1) and O,O-diphenyl, N-cyclooctyl phosphoramidate [*Ptychodiscus brevis* (PB-1)], were isolated from the *dinoflagellate*[8] and their formula's (Figure 1) were established on the basis of X-ray crystallography.

In order to study the structure–activity relationship, there was a need to synthesize these toxins containing phosphorus moiety. Moreover, the synthesis of P=O analogues of TG-1 is also not reported in the literature. Due to their unusual and unique formula, and their association with high degrees of activity, much attention was focused to study their biological aspects, only.[9] The non availability of TG-1 from the natural sources and biological activity shown by this compound prompted us to develop new strategy for the synthesis of TG-1 and its analogues. It is noteworthy to mention that P=O derivatives generally are more toxic than P=S derivatives, as has already been observed in case of paraoxane and parathion.[10] A literature search reveals that there has been little attention towards synthetic studies of TG-1 and its analogues. To the best of our knowledge, there is only one report for the synthesis of TG-1 using azeotropic distillation.[7b] This method, however, suffers from drawbacks such as use of carcinogenic solvent, long reaction times, requires chromatographic technique for purification, and gives rise to three minor unidentified impurities that reduced the yield of the desired product.

RESULTS AND DISCUSSION

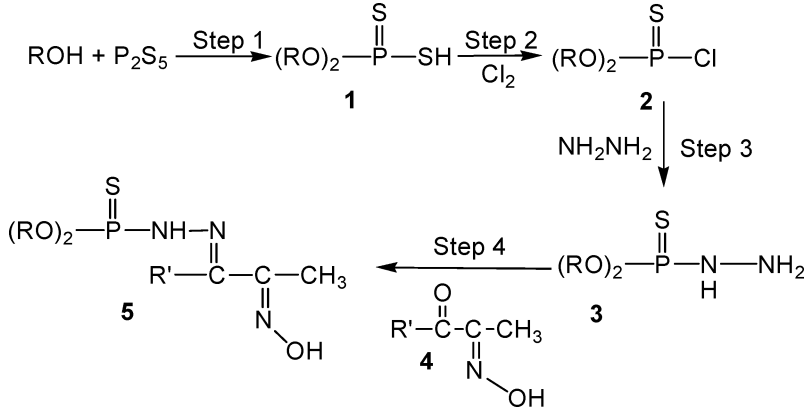
Retrosynthetic analysis revealed many synthetic routes, however, the most convenient and logical synthetic method for the synthesis of target compound (TG-1) is depicted in Scheme 1.

TG-1 was synthesised by condensing the phosphorahydrazide with the corresponding diketone monoxime (Scheme 2).



SCHEME 1

The intermediates **1–4** were synthesized by the reported methods.[10–13]However Step **4** of Scheme 2 appears simple, apparently, but it requires a chemoselective condensation of butane 2,3-dionemono (E) oxime and thiophosphoric acid hydrazide; Although a variety of reagents are available to transform carbon-nitrogen double bond.[14–18] However, the chemistry of condensation of carbonyl group with NH_2-Y (Y=OH, NH, $NHCONH_2$, etc.) reveals that an additional elimination reaction in which more basic nitrogen atom of amine adds to the carbonyl moiety and results in the formation of

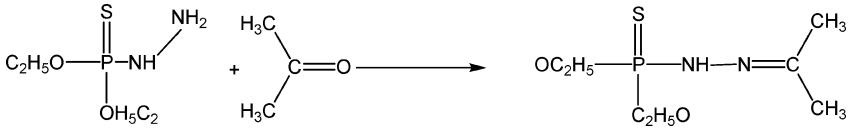


SCHEME 2 Synthesis of Tg1 **(5)** via use of thiophosphorichydrazides and butane 2,3 dione monoxime. Reaction Conditions: **1**, 5:1 mole ratio; benzene, 90°C, refluxed till P_2S_5 dissolved, under N_2 atmosphere,3–4 h **2**, solvent-CCl_4, temp.0°C, under N_2 atmosphere; 2–4 h **3**, mole ratio1:2; solvent-ethanol; temp. 0°C followed by r.t., 12 h; **4**, mole ratio 1:1: 1; acetonitrile, 2–3 h.

tetrahedral intermediate which gave carbon-nitrogen compounds after the elimination of water.[13] Furthermore, the removal of water is a reversible process and needs to be removed by azeotropic distillation.[19] Molecular sieves, dehydrating solvents, or the use of acid catalysts have been reported to facilitate such kind of reactions, as well.[20] The transformation of C=N double bond is challenging in TG-1 type of molecules essentially because of sensitive functionalities present in the molecule. These compounds are prone to Beckmann rearrangement due to the presence of free oximino functionality and/or can also undergo cyclization reaction through hydrazimino group. This is likely the reason that limited attempts have been made so far for the synthesis of TG-1 and its analogues. Recently, the use of insoluble inorganic materials as a condensing and water scavenger has received significant interest in organic chemistry. These heterogeneous reactions have advantages over the homogenous reactions due to ease of set-up and work-up, reaction time, high yields, and greater selectivity. Na_2SO_4–silica has been reported as condensing agent and as water scavengers for dehydration of alcohols.[21] In spite of the availability of various synthetic methods for transformation of C=N double bond, no attempt has been made to synthesize O, O-dialkyl, (E)-2-[1-methyl 2-oxopropylidene]phosphorohydrazidothiolate (E) oxime, and analogues by using Na_2SO_4-silica as a condensing agent and as water scavengers. In continuation of our recent work,[22] we report a new method for the synthesis of (*TG*-1) and its analogues via chemoselective condensation of thiophosphoric acid hydrazide and alkane dionemono (E) oxime using Na_2SO_4-silica resulting high yields of (TG-1) Scheme 2. This method efficiently afforded the TG-1 and its derivatives and allowed us to obtain excellent yields of the products in reduced reaction time. The condensing agent was prepared by mixing sodium sulfate solution with chromatographic silica gel and evaporating the water under reduced pressure by heating at 150°C .The condensing agent was dried at 200°C in a vacuum oven for 2 h (see Experimental section).

Initially, the reaction conditions were optimized by carrying out the reactions of diethyl thiophosphoric acid hydrazide with acetone as model reaction in the presence of different condensing agents such as silica, sodium sulfate, $CuSO_4$, $ZnSO_4$. SiO_2- Na_2SO_4, symctone clay, montmorillonite KSF clay, kiesel gel, SiO_2, Celite 521, kiesal gel, and activated carbon under various reaction conditions using different solvents. The reaction was monitored by TLC and GC to find out the consumption of diethyl thiophosphoric acid hydrazide and formation of the corresponding hydrazone (O,O-diethyl isopropylidenehydrazino thiophosphate). The result of this analysis showed that combination

TABLE I Optimization of Conditions for the Synthesis of O, O–Diethyl Isopropylidenehydrazino Thiophosphate



Entry	Condensing agent	Solvent	Mole (%)	Yield[a](%)
1.	Nil	benzene	nil	50[b]
2.	SiO_2	acetonitrile	100	57
3.	Na_2SO_4	acetonitrile	100	58
4.	Symctone clay	acetonitrile	10	14
5.	Montmorillonite KSF clay	acetonitrile	10	23
6.	SiO_2- Na_2SO_4	acetonitrile	10	86[c]
7.	Kiesel gel	acetonitrile	10	52
8.	Celite521	acetonitrile	10	16
9.	Activated carbon	DCM	10	NIL
14.	SiO_2- Na_2SO_4	acetonitrile	50	26
15.	SiO_2- Na_2SO_4	acetonitrile	75	68
16.	SiO_2- Na_2SO_4	acetonitrile	100	86
17.	SiO_2- Na_2SO_4	acetonitrile	120	89
18.	$ZnSO_4$	acetonitrile	100	34[d]
19.	$CuSO_4$	acetonitrile	100	27[d]
20.	SiO_2- Na_2SO_4	acetonitrile	100	36[e]

[a]Isolated yield; [b]Dean- Stark receiver was used and reaction was found incomplete in 2 h; [c]in ^{31}PNMR, a signal of diethyl thiophosphoric acid hydrazide (δ 73.20) disappeared, and a new signal at δ 68.43 appeared in entry 6; [d]a metal complex formed within 30–45 min; and [e]the reaction mixture was refluxed up to 10 h.

of SiO_2- Na_2SO_4 gave best results. However, the mole ratio of SiO_2-Na_2SO_4 plays a crucial role in increasing the yield of products. Equimolar ratio of anhydrous SiO_2-Na_2SO_4 was found an ideal choice as compared to others in terms of conversion and reaction time (Table I). It was also observed that all the reactions reached completion within 3–4 h when anhydrous SiO_2-Na_2SO_4 was used under reflux conditions. Extended reaction time did not have any significant change in the yield of products (Table I). The effects of solvent were also studied by using various solvents like THF, dioxane, acetonitrile, ethanol, diethyl ether, DCM, chloroform, and CCl_4; we observed that acetonitrile afforded the best results. Reactions were monitored by TLC, GC, and ^{31}P NMR at 162 MHz using $CDCl_3$. To explore the generality and scope of this condensing agent, various aldehydes and ketones with diverse structure were condensed with diethyl phosphoric hydrazides and the results are summarized in Table II.

Before applying the optimized reaction conditions for synthesis of TG-1 and its analogues, chemo-selectivity of the method was examined by performing two sets of control experiments under identical reaction conditions. In the first experiment, an equimolar mixture of benzophenone oxime and acetone were allowed to react with diethyl phosphoric acid hydrazide under similar reaction conditions and monitored by TLC and GC-Ms. The results showed that acetone reacted chemo-selectively and gave corresponding hydrazone in 83% yield, while there was no change in the mass spectrum of benzophenone oxime. Further, no Beckmann rearrangement product was also observed in IR and GC-Ms. In the second experiment, an equimolor mixture of benzophenone oxime and butane-2,3-dionemono-(E)-oxime were allowed to react with diethyl phosphoric acidhydrazide, the butane-2,3-dionemono-(E)-oxime reacted chemo-selectively and gave corresponding derivatives of TG-1. It indicated competitive condensation of butane-2,3-dionemono-(E)-oxime with diethyl phosphoric acid hydrazide. By following the above method, a variety of thiophosphoric acid hydrazides were reacted either with butane-2,3-dionemono-(E)-oxime or with 1-phenyl – 2-oxopropylidene-2-(E) oxime for the synthesis of TG-1 and its analogues, and the results are enumerated in Table III.

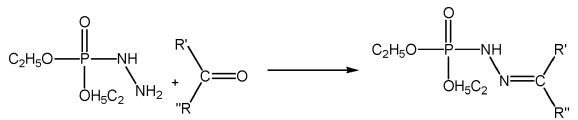
Since, it is known that compounds bearing P=O groups are more potent /active than their P=S derivatives. Therefore, to validate the reported fact, P=O analogues were also synthesized as per Scheme 3. The results of all the P=O derivatives are summarized in Table IV.

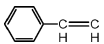
It is evident from Tables III and 4 that change in alkyl chain length in phosphorohydrazides influences the reaction time (entry 5a–5h and 8a–8l) to some extent. However, it was also observed that to butane-2, 3-dionemono (E) oxime reacted faster than 1-phenyl – 2-oxopropylidene-2-(E)-oxime. This is probably due to resonance of phenyl ring, which might reduce electrophillic nature of carbonyl carbon. The reactivity of phosphorohydrazides and thiophosphorohydrazides were also compared, the results of this study indicated that phosphoric acid hydrazides reacted faster compared to later one. The reaction of dianilino phosphoric acid hydrazide was observed slowest one as it took longer time (Table III, 8l). One of the unique features of this method is convenient work-up.

Bioassay

Any assay or estimation of any compounds for their biological activity in a particular organism or fish is defined as bioassay. All the compounds

TABLE II Synthesis of O,O-diethyl Alkylidenehydrazinophosphate using SiO_2- Na_2SO_4 as a Condensing Agent[a]



S. No	R′	R″	Time (h)	Yield (%)	M.p. (°C)	I.R. (cm^{-1})	1H-NMR ($CDCl_3$)δ (ppm)
1	CH_3	CH_3	2.00	84	44–45	3240 (NH),1643 (C=N), 1250(P=O), 1165, 1040, 965	1.71(t, 6H,J = 7.0); 2.25 (s, 3H); 2.29 (s,3H); 4.48 (m, 4H, $J_{H-H} \approx {}^3J_{P-}$ = 7.0); 8.86 (d, 1 H, J_{PH} = 24.68)
2	CH_3		2.30	89	63–64	3190 (NH), 1638 (C=N),1255(P=O), 1160, 1035, 970	1.72(t,6H,J = 7.10); 2.64 (s, 3H); 4.50(m,4H,$J_{H-H} \approx {}^3J_{P-H}$ = 7.10); 7.53–7.82(m,3H, Ar); 7.92–8.20 (m,2H,Ar); 9.20(d, 1H,J_{P-H} = 27.20)
3	H	i-C_3H_7	1.50	86	48–50	3170 (NH),1640 (C=N), 1260 (P=O), 1165, 1030, 980	1.44(t,6H,J = 7.0); 1.71 (t6H,J = 7.10); 2.75 (d,sep.,1H,J = 5.20); 4.50(m,4H,$J_{HH} \approx {}^3J_{PH}$ = 7.0); 7.50(d, 1H,CH=N,J = 5.0); 9.25 (d, 1H, J_{P-H} = 27.5)
4	H		1.65	88	84–86	3235(NH),1638 (C=N), 1255 (P=O), 1155, 1025, 965	1.76(t, 6H,J = 7.1); 4.53 (M4H,$J_{HH} \approx {}^3$ J_{PH} = 7.1); 7.55–7.82 (m, 3H); 7.86–8.15(m,2H); 8.31 (s,1H,CH=N); 9.45 (d,1H, J_{P-H} = 27.50)
5	H		2.75	82	99–102	3240(NH), 1625 (C=N), 1245 (P=O), 1160, 1035, 975	1.78(t,6H,J = 7.1); 4.55 (M, 4H, $J_{HH} \approx {}^3J_{PH}$ = 7.1); 7.20(d,1H,CH=CH,J = 3.85); 7.23(d,1H,CH=CH,J = 5.8); 7.50–7.93(m, 5H); 8.03–8.27 (m,1H,CH=N); 9.95 (d, 1H, J_{P-H} = 29.20 Hz)
6	CH_3	C_2H_5	2.15	89	54–56	3185(NH),1643 (C=N), 1250 (P=O), 1165, 1040, 965	0.98(t,3H,CH_3J = 7.0); 1.76(t,6H,J = 7.05); 2.20 (q,2H,CH_2-, J7 = 7.0); 4.46(m,4H,$J_{HH} \approx {}^3J_{PH}$ = 7.05); 8.86(d,1H,J_{PH} = 24.8)
7	C_2H_5	C_2H_5	2.30	88	54–56	3200(NH),1643 (C=N), 1250 (P=O), 1160, 1030, 960	0.98(t,6H,CH_3J = 7.0); 1.73 (t, 6H,J = 7.05); 2.20 (m,4H,CH_2-); 4.46 (qt, 4H, $J_{HH} \approx {}^3$ J_{PH} = 7.05); 8.86(d,1H,J_{PH} = 24.68Hz)
8	CH_3	CH_3	2.75	90[b]	144–146	3225(NH),1640 (C=N), 1255 (P=O), 1145, 1020, 955	2.25(s, 3H,Ch_3); 2.29(s, 3H, CH_3); 7.55–8.12 (m, 5H 2-Ar); 8.86 (d,1H, J_{P-H} = 24.8 Hz)

[a]All the reactions were performed using equimolar ratios of reactants and the condensing agent in acetonitrile at reflux temperature. The spectral data of all the compounds were found comparable with literature values; and [b]diphenyl phosphorohydrazidate was used at the place of diethyl phosphorohydrazidate.

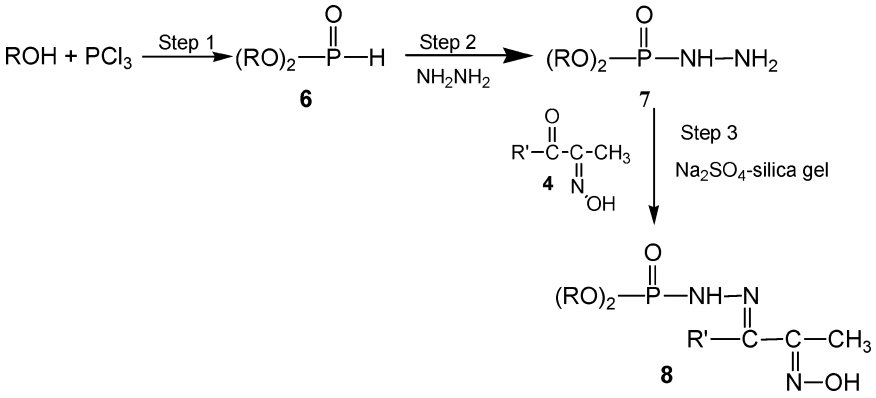
TABLE III Synthesis of O,O-dialkyl-2-(E)(1-alkyl-2-oxopropylidine) phosphorohydrazido thioate-(E)-oxime[a]

Entry	R	R′	Time (h)	m.p. (°C)	^{31}PNMR ($CDCl_3$)	Yield (%)
5a.	CH3	CH_3	2.00	61–62	67.62	86
5b.	C_2H_5	CH_3	2.15	67–69	65.32	80
5c.	*n*-C_3H_7	CH_3	2.30	80–82	64.74	86
5d.	*i*-C_3H_7	CH_3	2.30	79–80	61.50	87
5e.	*n*-C_4H_9	CH_3	2.75	89–91	63.90	82
5f	*n*-C_3H_7	C_6H_5	2.80	104–105	64.35	87
5g	*i*-C_3H_7	C_6H_5	3.00	100–101	61.19	84
5h	*i*-C_4H_9	CH_3	2.75	97–99	60.25	89

[a]Isolated yield; and [b]all the above reactions were performed by using 100 mole % of SiO_2-Na_2SO_4 in acetonitrile at reflux temperature. The reactions were monitored by silica TLC and ^{31} P NMR.

were subjected for biological evaluation against freshwater fish *R. daniconius* and their LC_{50} and LC_{90} were determined (see experimental). Table V showed the LC_{50} and LC_{90} values of TG-1 and its analogues. The results of fish toxicity are summarized in increasing order of LC_{50}value in Table V.

The LC_{50}value of parent synthetic toxin TG-1 was found to be 3.25 ppm. It indicates that at given concentration 50% mortality is observed However, out of 20 compounds, the toxicity of the first three compounds were found to be more or less similar (i.e., 3.0–3.32 ppm). The toxicity of seven analogues of synthetic toxin TG-1 have been observed to vary from 6.49–9.95 ppm, while rest of the compounds showed LC_{50} values ranging from 13.12–97.27 ppm (see Experimental section). The toxicity



SCHEME 3

TABLE IV Synthesis of O,O-dialkyl-2-(E) (1-alkyl-2-oxopropylidine) phosphorohydrazido–(E)-oxime[a]

Entry	R	R′	Time (h)	m.p. (°C)	^{31}PNMR ($CDCl_3$)	Yield (%)
8a.	CH_3	CH_3	1.75	52–53	3.20	88
8b.	C_2H_5	CH_3	2.00	57–59	2.89	85
8c.	n-C_3H_7	CH_3	2.20	62–64	2.37	82
8d.	i-C_3H_7	CH_3	2.30	76–77	1.51	85
8e.	n-C_4H_9	CH_3	2.50	82–83	1.31	82
8f.	n-C_3H_7	C_6H_5	2.60	110–111	2.07	87
8g.	i-C_3H_7	C_6H_5	2.75	107–108	1.49	87
8h.	i-C_4H_9	CH_3	2.75	90–91	1.65	84
8i.	C_6H_5	C_6H_5	3.25	156–157	−0.65	87
8j.	C_2H_5	C_6H_5	2.50	87–88	2.24	83
8k.	C_6H_5NH	C_6H_5	4.50	235–237	−3.71	79
8l.	C_6H_5	CH_3	2.75	148–150	−0.34	85

[a]Isolated yield, All the above reactions were performed by using 10 mole % of SiO_2-Na_2SO_4 in acetonitrile. The reactions were monitored by silica TLC and ^{31}P NMR.

of oxo analogues are in some instances slightly higher than their thio analogues. Probably, this may be due to higher binding characteristics of the former with the target enzyme.

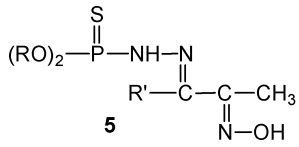
CONCLUSION

In conclusion, we report a general and highly efficient method for the synthesis of biologically active TG-1 and its P=O analogues by condensation of thiophosphoric acid hydrazides as well as and phosphoric acid hydrazides in excellent yields using thermally stable condensing agent (SiO_2- Na_2SO_4). This method offers several advantages over earlier reported method in terms of versatility, clean reaction, easy work up, recyclability of condensing agent, avoids the use of column chromatography for purification and shorter reaction times.

EXPERIMENTAL

All the solvents were dried according to published methods and distilled before use. The reactions were carried out in oven-dried glassware. Analytical thin layer chromatography (TLC) was performed on aluminum plates with Merck Kieselgel 60F254 and visualized by UV irradiation (254 nm) or with iodine. The purity of compounds was further checked on a country make Chemito GC model 1000 instrument. It was used with flame ionization detector (FID). The capillary column

TABLE V Toxicity of TG-1(5 and 8) and Its Analogues against Fresh Water Fish *Rasbora Daniconius*



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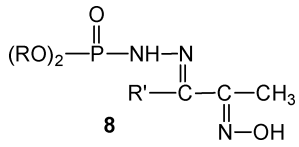

8

S. no.	R	R′	X	LC_{50}(ppm)	LC_{90}(ppm)
1.	C_3H_7	CH_3	O	3.00	4.50
2.	C_3H_7	CH_3	S	3.25	5.43
3.	C_2H_5	CH_3	O	3.32	5.69
4.	C_2H_5	CH_3	S	6.49	9.90
5.	CH_3	CH_3	O	7.06	12.45
6.	CH_3	CH_3	S	8.13	12.94
7.	C_3H_7	C_6H_5	O	9.60	12.64
8.	C_6H_5	CH_3	O	9.68	13.51
9.	C_3H_7	C_6H_5	S	9.71	14.22
10.	i-C_3H_7	CH_3	O	9.95	16.96
11.	i-C_3H_7	CH_3	S	13.12	18.15
12.	i-C_3H_7	C_6H_5	O	19.98	26.76
13.	i-C_3H_7	C_6H_5	S	25.48	33.46
14.	n-C_4H_9	CH_3	S	25.53	35.39
15.	i-C_4H_9	CH_3	O	27.74	38.13
16.	C_6H_5	C_6H_5	O	29.01	39.19
17.	i-C_4H_9	CH_3	S	33.28	68.00
18.	C_2H_5	C_6H_5	O	43.62	51.27
19.	n-C_4H_9	C_6H_5	O	95.99	110.35
20	C_6H_5NH	C_6H_5NH	O	97.27[a]	130.67

[a]The compound was dissolved in DMSO.

(30 m × 0.25 mm I.D-BP5) packed with 5% phenyl and 95% dimethyl polysiloxane (SGE) coated on fused silica was employed. The injection port and detector block were maintained at 280°C and 260°C respectively and the column oven was at programmed temperature profile started at 50°C, ramped up to 280°C at 25°C/min. Nitrogen was used as a carrier gas (at a flow rate of 30 ml/min). Air for FID was supplied at 300 ml/min and hydrogen at 30 ml/min. In all analyses, 1 μl sample was injected and peaks recorded on computerized data acquisition station. Melting points were determined on a hot stage microscope and are uncorrected. FT-IR spectra were recorded on Bruker FT-IR spectrometer model Tensor^{TM} 27 on KBr disk. ^{1}H and ^{31}P NMR spectra were recorded on Bruker DPX Avance 400 MHz FT- NMR in $CDCl_3$ or $(CD_3)_2SO$ at ambient temperature using tetramethylsilane as an internal standard for ^{1}H and 85% H_3PO_4 as an external standard for ^{31}P

NMR. Chemical shifts (δ) are given in parts per million (ppm) and coupling constants (J) are given in Hertz (Hz). GC- MS data were recorded on Varian 3400 GC coupled to a TSQ 7000 mass spectrometer (Finnigan Mat). In order to operate GC the injector temperature 250°C, Transfer line temperature 280°C, Column temperature programming 50°C (2 min) @ 10°C/min to 280°C (5 min), carrier gas helium at pressure of 10 psi conditions were used. To obtain EI mass spectra Ion source pressure 1.5×10^{-6} torr, source temperature 150°C, electron energy 70 eV and emission current 400 μA were used as the operating conditions. To perform chemical ionization (CI) technique, the ion source pressure with methane as the reagent gas 1.5×10^{-3} torr, source temperature 150°C, electron energy 100 eV and emission current 300 μA were maintained to operate the mass spectrometer. Elemental analysis was performed on elemental analyzer Carlo Erba Instrumantazione Model NOD1106 by using benzanilide as a reference compound.

Biological Evaluation against Freshwater Fish, *R. Daniconious*

To study the biological activity/toxicity of synthetic toxin TG-1, PB-1 and their various analogues as fish toxin freshwater fish *Rasboradaniconius* were collected, from fresh water ponds present around Gwalior. For each biological evaluation, 20 fish were released in enamel bowl containing 3 L of water with different concentration of compounds used under this study. Before performing actual experiments fish were conditioned with non-chlorinated water under laboratory conditions (28°C ± 2°C). For each experiment, three replicates with controls (each of 20 fish) were used. Fish were subjected to various concentrations of compounds continuously for 96 h. After this exposure period, data were recorded on mortality of fish under various toxic stresses. Data on various concentrations and corresponding mortality of fish were subjected to probit analysis.[23] For the determination of lethal concentration for 50% and 90% mortality, data have been subjected to determine fiducial limit for LC_{50} and LC_{90}, and chi square value was calculated to ascertain the heterogeneity among the fish population taken for experiments. To conduct the experiment, compounds were dissolved in ethanol and same amount of ethanol was used for control experiments, which were also conducted simultaneously.

Preparation and Characterization of Silica- Na_2SO_4

Silica- Na_2SO_4 was prepared by combination of silica (column chromatography 10.0 g, 166.0 mmol) and anhydrous Na_2SO_4 (20.0 g, 140.0 mmol) in a mortar and pestle by grinding together until a fine,

homogenous powder was obtained (10–15 min). It was mixed with 150 ml of distilled water and stirred for 1 h at room temperature and then water was removed under vacuum using Heidolph rotary evaporator till dryness. It was shaken with 100 ml acetonitrile, filtered, and washed with 3 × 25 ml acetonitrile. It was further dried under vacuum at 150°C for 2 h and stored in a stoppard flask under desiccators. However, in order to know the nature of Silica- Na_2SO_4, microstructural studies were performed by scanning electron microscope (SEM). It was observed that silica was finely and uniformly distributed on the Na_2SO_4.

General Procedure (5a–5h)—Typical Example

The solution of diacetylemonoxime (10.01 g, 100.0 mmol) in acetonitrile (20 ml) was added to a suspended solution of O,O-dipropyl thiophosphorichydrazide (18.40 g, 100.0 mmol) and anhydrous silica-Na_2SO_4 (20.6 g, 100.0 mmol) in 100 ml acetonitrile. The reaction mixture was refluxed with constant stirring and monitored periodically by TLC and ^{31}P NMR. After complete consumption of O,O-dipropyl thiophosphorichydrazide (4 h), the reaction mixture was cooled at room temperature and was filtered off. The solvent was removed in rotary evaporator to afford the desired crude product, which was re-crystallized from DCM-ether mixture (6:4 vol/vol). Yield; (21.36g, 80%); m.p.67–69°C. Spectral data of newly synthesized compounds are given in the following.

5a O,O-Dimethyl,2-(1-methyl 2-Oxopropylidine) Phosphorohydrazidothioate (E)-oxime

^1H NMR ($CDCl_3$); δ = 6.8 (S,1H,NOH, *exchangeable*), 5.62 (d,1H,NH,J_{P-H} = 26.20Hz, *exchangeable*), 3.75(d, 6H, CH_3J_{H-P} = 12.21Hz), 2.31(S, 3H, CH_3), 2.15(S,3H,CH_3); IR(KBr disc); $\upsilon(cm^{-1})$ = 3450(-OH), 3220(NH), 2930(C-H),1660(-C=N-), 1590(NH, *def*), 1150, 1025, 970(P-O-C), 730(P=S); GC-MS(EI)% = 240($M+H^+$ 4.2), 239(M^+ 6.8), 222(22.0), 191(33), 160(16.5), 115(100), 98(65); Anal. calcd. for $C_6H_{14}N_3O_3PS$: C, 30.13; H, 5.85; N, 17.57. Found: C, 30.35; H, 6.08; N, 17.28.

5b O,O-Diethyl-2-(1-methyl-2-oxopropylidene) phosphorohydrazidothioate-(E)-oxime

^1H NMR ($CDCl_3$); δ = 7.65 (S,1H,NOH, *exchangeable*), 5.69 (d, 1H, NH,J_{P-H} = 25.6Hz, *exchangeable*),4.1 (m, 4H, CH_2O,J_{H-H} = J_{H-P} = 7.05 Hz), 2.01(S,3H,CH_3), 1.91(S,3H,CH_3), 1.20(t, 6H, CH_3,J_{H-H} = 7.10Hz); IR KBr (disc) υ (cm^{-1}); 3420(OH), 3245(NH), 2860(str C-H), 1625(>C=N-), 1590(N-H *def*), 1145, 1025(P-O-C), 735(P=S), GC-MS (EI) m/z(%); 268($M+H^+$, 100), 267(M^+, 7.4), 250(6.2), 184(4.2), 153

(2.7), 125(5.8), 121(5.6), 114(5.3), 98 (2.8), 97(10.3); Anal. calcd. for $C_8H_{18}N_3O_3PS$: C, 35.95; H, 6.74; N, 15.73. Found: C, 36.21; H, 6.98; N, 15.95.

5c O,O-Dipropyl-2-(1-methyl-2-oxopropylidine) phosphorohydrazidethioate-(E)-oxime

^{1}H NMR ($CDCl_3$); $\delta = 7.96$(S,1H,NOH *exchangeable*), 6.75(d, 1H, NH, $J_{P\text{-}H} = 26.16$Hz, *exchangeable*), 4.09(m, 4H, CH_2O, $J_{H\text{-}P} = 6.68$Hz) 2.08(S,3H,CH_3), 1.96 (S,3H,CH_3), 1.74(m,4H,CH_2, $J_{H\text{-}H} = 6.76_{Hz)}$, 0.96(t,6H,$CH_3$, $J_{H\text{-}H} = 6.72$Hz); IR KBr disc υ (cm^{-1}), 3410(-OH), 3225(-NH), 2850(C-H), 1630(C=N), 1595(-NH *def.*), 1135, 1020(P-O-C), 750(P=S); GC-MS(EI)m/z(%); 296($M+H^+$, 71.8), 295(M^+,82.8), 278(16.2), 253(32.5), 236(12), 220(10), 211(58.9), 194(17.3), 178(24.3), 153(22.5), 139(34.7), 116(40.7), 115(78.1), 114(95.2), 98(100), 97(42.8) Anal. calcd. for $C_{10}H_{22}N_3O_3PS$: C, 40.67; H, 7.45; N, 14.23. Found: C, 40.81; H, 7.75; N, 14.47.

5d O,O-Diisopropyl-2-(1-methyl-2-oxopropylidine) phosphorohydrazido thioate (E)-oxime

^{1}H NMR ($CDCl_3$); $\delta = 7.8$ (S, 1H, NOH, *exchangeable*), 6.02(d, 1H, NH, $J_{P\text{-}H} = 25.96$Hz, *exchangeable*),4.60(m, 2H, CH, $J_{H\text{-}H} = 6.68$Hz), 2.08(S, 3H, CH_3), 1.95(S, 3H, CH_3), 1.30(d,d, 12H, CH_3, $J_{H\text{-}H} = 6.28$Hz; IR KBr disc υ (cm^{-1}), 3400(-OH), 3215(-NH), 2860(C-H), 1635(C=N), 1590(NH *def*) 1125, 1030(P-O-C), 760(P=S), 296($M+H^+$, 3.8), 295(M+, 50.9), 278(46.9), 236(6.5), 220(54), 211(8.9), 194(27.3), 178(86.3), 153(12.5), 139(33.7), 116(10), 115(88.7), 114(85.2), 98(100), 97(28.8); Anal calcd. for $C_{10}H_{22}N_3O_3PS$: C, 40.67; H, 7.45; N, 142.3. Found: C, 40.97; H, 7.98; N. 14.88.

5e O,O-Dibutyl 2-(1-methyl 2–oxopropylidene) hydrazidothioate-E-oxime

^{1}H NMR ($CDCl_3$); $\delta = 6.94$(S, 1H, NOH, *exchangeable*), 5.80(d, 1H, NH, $J_{P\text{-}H} = 26.62$Hz, *exchangeable*), 4.02(m, 4H, CH_2, $J_{H\text{-}H} = J_{P\text{-}H} = 6.62$Hz, 2.11(S,3H,$CH_3$), 1.98(S,3H,$CH_3$), 1.83(m, 8H,$CH_2$) 0.97(t, 6H, CH_3, $J_{H\text{-}H} = 6.48$Hz); FT-IR KBr(disc) υ (cm^{-1}); 3440(-OH), 3250(NH), 2850(C-H), 1632(C=N), 1600(N-H *def*), 1025, 940(P-O-C), 750(P=S); GC-MS(EI)m/z (%); 324($M+H^+$, 3.1), 323(M^+, 5.8), 306(15.5), 267(18.5), 234(12), 250(10.8), 211(11)194(20.5), 178(6.5), 115(75), 98(100),97(8.5) Anal. calcd. for $C_{12}H_{26}N_3O_3PS$: C, 44.58; H, 8.05; N, 13.00. Found: C, 44.25; H, 8.30; N, 13.28.

5f O,O-isodibutyl,2-(1-methyloxopropylidene) hydrazidothioate-E-oxime

^{1}H NMR ($CDCl_3$); δ = 7.58(S, 1H, NOH,*exchangeable*), 6.57(d, 1H, NH, J_{P-H} = 26.02Hz *exchangeable*), 4.03(m, 4H, CH_2, J_{H-H} = J_{P-H} = 6.50Hz), 2.13(S, 3H, CH_3), 1.96(S, 3H, CH_3), 1.88(m, 2H, CH), 1.32(d, 12H, CH_3), 6.57(d, 1H, NH),; FT-IR KBr (disc) υ (cm^{-1}); 3420(-OH), 3250(-NH), 2880(C-H), 1640(C=N), 1590(-NH def), 1140, 980(P-O-C), 760(P=S) GC-MS(EI) m/z(%); $M+H^+$, 2.8),323(M^+, 4.2), 306(12.7), 267(20.3), 234(14.5), 211(18), 194(22.6), 178(8.2), 115(71), 98(100), 97(9.7); Anal. calcd. for $C_{12}H_{26}N_3O_3PS$: C, 44.58; H, 8.05; N, 13.00. Found: C, 44.88; H, 8.35; N, 13.23.

5g O,O-Dipropyl 2-(1-Phenyloxopropylidine) hydrazido thioate (E) oxime

^{1}H NMR ($CDCl_3$); 7.78(S,1,NOH, *exchangeable*), 7.32(m,5H, C_6H_5), 6.52(S,1H,NH, J_{P-H} = 26.40Hz, *exchangeable*), 4.12(m, 4H, CH_2O, J_{H-P} = 6.60Hz), 1.94 (S,3H,CH_3), 1.74(m,4H,CH_2, J_{H-H} = 6.76Hz), 0.95(t,6H,CH_3, J_{H-H} = 6.70Hz); FT-IR KBr(disc) υ (cm^{-1});3425(-OH), 3230(-NH), 2875(C-H), 1625(C=N), 1585(-NH,def.)1125, 990(P-O-C), 745(P=S); GC-MS(EI)m/z(%) 357 (M^+, 36.2), 340(3.55), 298(3.3), 273(3.5), 240 (3.5), 202 (5.8), 178 (13.8), 177(21.8), 160(34.6),104(8.2), 77(45.0); Anal. calcd. for $C_{15}H_{24}N_3O_3PS$: C, 50.42; H, 6.72; N, 11.76. Found: C, 49.82; H, 6.93; N, 11.58.

5h O,O-Diisopropyl 2-(1-Phenyl-2-oxopropylidine) hydrazidothioate-E-oxime

^{1}H NMR ($CDCl_3$); 7.73(S,1,NOH, *exchangeable*), 7.32(m,5H, C_6H_5), 6.67(S,1H,NH, J_{P-H} = 26.79Hz,*exchangeable*), 4.25(m, 2H, CH, J_{H-H} = 6.88Hz),1.94(S, 3H, CH_3), 1.32 (d,d,12H, CH_3, J_{H-H} = 6.28Hz);FT-IR(KBr) disc υ (cm^{-1}), 3400 (OH), 3210(NH), 2900 (C-H), 1640(C=N), 1590(NH *def.*)1120, 1050(P-O-C), 760(P=S), GC-MS (EI)m/z (%) 357(M^+, 30.2), 340(5.0), 298(2.3), 273(4.5),177(18), 160(32.6),104(8.2), 77(42.7); Anal. calcd. for $C_{15}H_{24}N_3O_3PS$: C, 50.42; H, 6.72; N, 11.76. Found: H, 6.98; N, 11.65.

General Procedure (8a–8l)—Typical Example

The solution of diacetylemonoxime (10.01 g, 100.0 mmol) in acetonitrile (20 ml) was added to a suspended solution of O,O-dialkyl phosphoric acid hydrazide (100.0 mmol) and anhydrous silica-Na_2SO_4(20.6 g, 100.0 mmol) in 100 ml acetonitrile. The reaction mixture was refluxed with constant stirring and monitored periodically by TLC and ^{31}P NMR. After complete consumption of corresponding phosphoric acid

hydrazide(as per time given in Table III), the reaction mixture was cooled at room temperature and was filtered off. The solid product was washed with 2 × 15 ml acetonitrile. The filtrate and washings were combined and the solvent was removed in rotary evaporator to afford the desired crude product, which was triturated with ether to give solid white product. Spectral data of newly synthesized compounds are given, following.

8a O,O-Dimethyl,2-(1-methyl oxopropylidine) Phosphorohydrazido(E)-oxime

^{1}H NMR ($CDCl_3$); δ = 8.41 (S,1H,NOH, *exchangeable*), 6.20(d,1H,NH, J_{P-H} = 25.20Hz, *exchangeable*), 3.80(d, 6H, CH_3 J_{H-P} = 12.0Hz), 2.32 (S, 3H, CH_3), 2.21(S,3H,CH_3); IR(KBr disc); υ(cm^{-1}) = 3470 (-OH), 3270(NH), 2925(C-H),1640(-C=N-), 1570(NH, *def*), 1255(P=O), 1045,960 (P-O-C),; GC-MS(EI)% = 224($M+H^+$ 6.2), 223(M^+ 7.8), 206(27), 193(5.3), 163(18.5), 115(100**),** 109(31) 98(65**);** Anal. calcd. for $C_6H_{14}N_3O_4P$: C, 32.28; H, 6.27; N, 18.83. Found: C, 32.05; H, 6.58; N, 18.58.

8b O,O-Diethyl-2-(1-methyl-2-oxopropylidene) phosphorohydrazido-(E)-oxime

^{1}H NMR ($CDCl_3$); δ = 8.15 (S,1H,NOH, *exchangeable*), 5.75 (d, 1H, NH,J_{P-H} = 26.26Hz, *exchangeable*),4.21(m,4H,CH_2O,J_{H-H} = J_{H-P} = 7.0Hz), 2.10(S,3H,CH_3), 2.01(S,3H,CH_3), 1.23(t, 6H, CH_3, J_{H-H} = 7.0Hz); IR KBr (disc) υ (cm^{-1}); 3425(OH), 3255(NH), 2870(str C-H),1635(>C=N-),1580(N-H*def*),1245(P=O),1035,950(P-O-C), GC-MS (EI) m/z(%); 252($M+H^+$, 7.3), 251(M^+, 3.4), 234(6.62), 206(24.2), 195(11.20, 178 (32.7), 115(85.3), 98 (42.8); Anal. calcd. for $C_8H_{18}N_3O_4P$: C, 38.24; H, 7.17; N, 16.73. Found: C, 37.15; H, 6.98; N, 16.95.

8c O,O-Dipropyl-2-(1-methyl-2-oxopropylidine) phosphorohydrazide-(E)-oxime

^{1}H NMR ($CDCl_3$); δ = 7.59(S,1H,NOH *exchangeable*), 6.15(d, 1H, NH, J_{P-H} = 26.40Hz, *exchangeable*), 4.20(m,4H,CH_2O,J_{H-P} = 7.08Hz), 2.18 (S,3H,CH_3), 1.98(S,3H,CH_3), 1.75 (m,4H,CH_2,J_{H-H} = 6.97$_{Hz}$), 0.96 (t,6H,CH_3,J_{H-H} = 6.87Hz);IR KBr disc υ(cm^{-1}), 3425(-OH), 3230(-NH), 2860(C-H), 1635(C=N), 1585(-NH*def.*), 1235(P=O), 1020,940(P-O-C), GC-MS(EI)m/z(%); 280($M+H^+$,12.28), 279(M^+,8.8), 264(18.42), 262(9.32), 237(22),220(15.40), 195(16.73), 115(34.7),98(80); Anal. calcd. for $C_{10}H_{22}N_3O_4P$: C, 43.07; H, 7.88; N, 15.05. Found: C, 43.40; H, 8.02; N, 15.24.

8d O,O-Diisopropyl-2-(1-methyl-2-oxopropylidine) phosphorohydrazido (E)-oxime

^{1}H NMR ($CDCl_3$);δ = 7.58(S,1H,NOH, *exchangeable*),6.10(d,1H,NH, $J_{P\text{-}H}$ = 25.76Hz, *exchangeable*), 4.65(m,2H,CH,$J_{H\text{-}H}$ = 6.65Hz), 2.09 (S,3H, CH_3),1.96 (S,3H,CH_3), 1.32 (d,d,12H,CH_3,$J_{H\text{-}H}$ = 6.45Hz; IR KBr disc υ (cm^{-1}),3415(-OH),3225(-NH),2860(C-H), 1625(C=N), 1575(NH*def*), 1245(P=O),1030,950(P-O-C),GC-MS(EI)m/z(%);280 ($M+H^+$,4.8), 279 (M^+,24.4), 264(2.5), 237(16), 222(7.9), 195(37.3), 178(26.3), 137(12.85), 115(15.7), 114(12.2), 99(10.30), 98(100); Anal. calcd. for $C_{10}H_{22}N_3O_4P$: C, 43.07; H, 7.88; N, 15.05. Found: C, 42.95; H, 7.68; N, 14.91.

8e O,O-Dibutyl 2-(1-methyloxoprophlidine) hydrazido-E-oxime

^{1}H NMR ($CDCl_3$); δ = 7.54(S, 1H, NOH, *exchangeable*), 6.08(d, 1H, NH, $J_{P\text{-}H}$ = 25.74Hz, *exchangeable*), 4.22(m, 4H, CH_2, $J_{H\text{-}H}$ = $J_{P\text{-}H}$ = 6.82Hz, 2.10(S,3H,CH_3), 1.98(S,3H,CH_3), 1.85(m, 8H,CH_2) 0.97(t, 6H, CH_3, $J_{H\text{-}H}$ = 6.78Hz); FT-IR KBr(disc) υ (cm^{-1}); 3440(-OH), 3260(NH), 2850(C-H), 1625(C=N), 1580(N-H *def*), 1250(P=O) 1035, 950(P-O-C),; GC-MS(EI)m/z(%); 308($M+H^+$,6.7), 307(M^+, 3.8), 290(13.5),251(15.8), 234(14), 195(22.25),115(45),98(87), Anal. calcd. for $C_{12}H_{26}N_3O_4P$: C, 46.90; H, 8.46; N, 13.68. Found: C, 46.75; H, 8.72; N, 13.80.

8f O,O-Dipropyl 2-(1-phenyl oxopropylidine) hydrazido (E) oxime

^{1}H NMR ($CDCl_3$); 7.78(S,1,NOH, *exchangeable*), 7.43(m,5H, C_6H_5), 6.42(S,1H,NH, JP-H = 25.74Hz, *exchangeable*), 4.32(m, 4H, CH_2O, $J_{H\text{-}P}$ = 6.76Hz), 1.95 (S,3H,CH_3), 1.75(m,4H,CH_2, $J_{H\text{-}H}$ = 6.75Hz), 0.97(t,6H,CH_3, $J_{H\text{-}H}$ = 6.70Hz); FT-IR KBr(disc) υ (cm^{-1});3425(-OH), 3240(-NH), 2900(C-H), 1625(C=N),1575(-NH,def.)1245(P=O),1025, 950(P-O-C); GC-MS(EI)m/z(%) 342($M+H^+$, 15.94) 341(M^+, 26.2), 299(13), 257(23.5), 256(23.5), 240(12.18), 178(3.8), 177(12.8), 176(20.6), 160(100), 130(25.0), 125(17), 105(15.5), 104(18.5), 103(27), 94(98), 77(29), Anal. calcd. for $C_{15}H_{24}N_3O_4P$: C, 52.79; H, 7.03; N, 12.32. Found: C, 52.58; H, 6.90; N, 12.08.

8g O,O-Diisopropyl 2-(1-phenyl-2-oxopropylidine) hydrazido-E-oxime

^{1}H NMR ($CDCl_3$); 7.87(S,1,NOH, *exchangeable*), 7.38(m,5H,C_6H_5), 6.37(S,1H,NH,$J_{P\text{-}H}$ = 26.12Hz, *exchangeable*), 4.24(m,2H,CH,$J_{H\text{-}H}$ = 6.78Hz), 1.95(S,3H,CH_3),1.33 (d,d,12H,CH_3,$J_{H\text{-}H}$ = 6.20Hz); FT-IR (KBr) discυ(cm^{-1}),3420(OH),3230(NH),2900(C-H), 1628(C=N), 1580 (NH*def*.), 1248(P=O), 1050, 930(P-O-C), GC-S(EI)m/z(%) 342($M+H^+$, 8.64) 341(M^+,14.28), 299(9.24), 257(21.55), 256(28.5), 240(12.18),

177(10.50), 160(86), 130(21.0), 125(11.75), 105(9.5), 104(12.5), 94(98), 77(11.50), Anal.calcd. for $C_{15}H_{24}N_3O_4P$: C, 52.79; H, 7.03; N, 12.32. Found: C, 53.02; H, 7.23; N, 12.48.

8h O,O-isodibutyl,2-(1-methyloxopropylidene) hydrazido-E-oxime

^{1}H NMR ($CDCl_3$); δ = 7.58(S, 1H, NOH, *exchangeable*), 6.69(d, 1H, NH, JP-H = 25.76Hz *exchangeable*), 6.57(d, 1H, NH), 4.23(m, 4H, CH_2, JH-H = JP-H = 6.50Hz), 2.13(S, 3H, CH_3), 1.99(S, 3H, CH_3), 1.81(m,2H,CH), 1.30(d, 12H, CH_3),; FT-IR KBr (disc) υ (cm^{-1}); 3420(-OH), 3250(-NH), 2880(C-H), 1640(C=N), 1590(-NH def), 1140, 980(P-O-C), GC-MS(EI)m/z (%); 308($M+H^+$, 15.14), 307(M^+, 8.13), 290(34.25),251(19.25), 234(22.87), 195(17.22),115(39.62),98(77), Anal. calcd. for $C_{12}H_{26}N_3O_4P$: C, 46.90; H, 8.46; N, 13.68. Found: C, 47.15; H, 8.32; N, 13.48.

8i O,O-Diphenyl 2-(1-phenyl-2-oxopropylidine) hydrazido-E-oxime

^{1}H NMR ($CDCl_3$); δ = 7.86(s,1H,NOH, *exchangeable*)), 7.5(m,15H, C_6H_5), 1.9(s,3H,CH_3), 6.32(S,1H,NH, J_{P-H} = 25.74Hz, *exchangeable*),); FT-IR KBr (disc) υ (cm^{-1}); 3420(-OH), 3250(-NH), 2880(C-H), 1640(C=N), 1590(-NH def), 1240(P=O), 1030,930(P-O-C),; GC-MS(EI) m/z(%) 409(M^+, 1.54),392(1.28), 249(3.54), 248(2.1), 235(1.75), 170(1.50), 160(26), 159(63), 130 (15.75), 118(22.5) 105(22.5), 104(19), 103(27), 94(100), 77(29.4), Anal. Calcd for $C_{21}H_{20}N_3O_4P$: C, 66.61; H, 4.88; N, 10.26. Found: C, 61.75; H, 5.00; N, 10.05.

8j O,O-Diethyl-2-(1-phenyl-2-oxopropylidene) phosphorohydrazido-(E)-oxime

^{1}H NMR ($CDCl_3$); δ = 8.12 (S,1H,NOH, *exchangeable*), 7.38(m,5H, C_6H_5), 5.75 (d, 1H, NH,J $_{P-H}$ = 26.18Hz, *exchangeable*),4.28 (m, 4H, CH_2O, $J_{H-H} = J_{H-P}$ = 7.0 Hz), 1.99(S,3H,CH_3), 1.24(t, 6H, CH_3, J $_{H-H}$ = 7.0Hz); IR KBr (disc) υ (cm^{-1}); 3440(OH), 3260(NH), 2880(str C-H), 1625(>C=N-), 1570(N-H *def*), 1255(P=O), 1035,940(P-O-C), GC-MS (EI) m/z(%); 314($M+H^+$, 17.3), 313(M^+, 8.4), 296(12.60), 285(20.2), 287(7.20), 257(22), 240(7.75), 177 (82.7), 178(25.13), 160 (12.8), 159(63), 130 (15.75), 118(22.5) 105(22.5), 104(19), 103(27), 94(100), 77(29.4); Anal. calcd. for $C_{13}H_{20}N_3O_4P$: C, 49.84; H, 6.38; N, 13.42. Found: C, 50.12; H, 6.78; N, 13.29.

8k O,O-Dianilino-2-(1-phenyl2-oxopropylidene) phosphorohydrazido-(E)-oxime

^{1}H NMR (DMSO-d_6); δ = 11.36(s,1H,NOH, *exchangeable*)), 8.51(d,2H, C_6H_5NH, J = 9Hz), 7.98(d,1H,NH, J_{P-H} = 25.34Hz), 7.3–6.27(m, 15H, Ar), 5.78(S,1H,NH, J $_{P-H}$ = 25.34Hz, *exchangeable*),);

FT-IR KBr (disc) υ (cm^{-1}); 3420(-OH), 3360, 3150(-NH), 2870(C-H), 1635(C=N), 1590(-NH def), 1235P=O), 1030,930(P-O-C),; Mass(D.P.)(EI)m/z(%) 408(M^+, 3.74),407(M^+,2.1), 390(6.78), 330(2.54), 248(2.1), 315(14.75), 253(18.7),223(2.3), 177(12.50), 160(20.8), 94(90),93(48), 77(22.4), Anal. calcd. for $C_{21}H_{22}N_5O_2P$: C, 61.91; H, 5.40; N, 17.19. Found: C, 61.78; H, 5.68; N, 17.40.

8l O,O-Diphenyl-2-(1-methyl-2-oxopropylidene) phosphorohydrazido-(E)-oxime

^{1}H NMR ($CDCl_3$); δ = 7.83(s,1H,NOH, *exchangeable*)), 7.45(m,10H, C_6H_5), 6.32(S,1H,NH, J $_{P-H}$ = 25.63Hz, *exchangeable*), 2.10(S, 3H, CH_3), 1.93(s,3H,CH_3); FT-IR KBr (disc) υ (cm^{-1}); 3420(-OH), 3250(-NH), 2880(C-H), 1640(C=N), 1590(-NH def), 1240(P=O), 1030, 930(P-O-C); GC-MS(EI)m/z(%)348($M+H^+$,24), 347(M^+,16.5), 330(21.54), 254(13.54), 248(2.1), 233(8.75), 132 (15.75), 114(6.22) 98(30), 94(100), 77(12), Anal. calcd. for $C_{16}H_{18}N_3O_4P$: C, 55.33; H, 5.18; N, 12.10. Found: C, 55.10; H, 5.00; N, 12.38.

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