

Full Paper

Novel and Efficient Synthesis of *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido Oximes. Part 3

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Abstract: A novel and efficient method has been developed for the synthesis of *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oximes **5**. The reactions involve the condensation of diacetylmonoxime and *N,N*-dialkylamino-*O*-alkylphosphorohydrazides in the presence of activated silica and give the corresponding target oximes in excellent yields under mild conditions.

Keywords: Hydrazides, diacetylmonoxime, marine fish toxin, phosphorohydrazido oximes.

Introduction

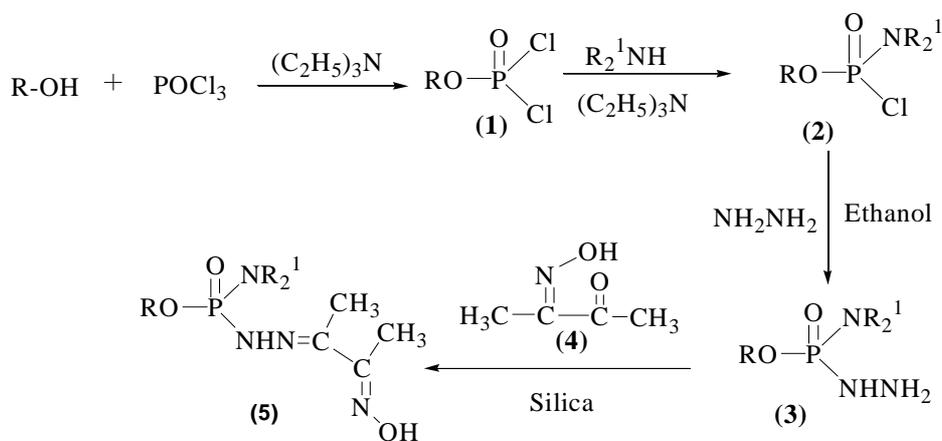
Two unusual naturally occurring phosphorus-containing fish toxins were isolated for the first time from *Gymnodinium breve* and their structures established as *O,O*-dipropyl-(*E*)-2-(1-methyl-2-oxopropylidene)phosphorohydrazidothiolate-(*E*)-oxime [1] and *O,O*-diphenylcyclooctylphosphoramidate (PB-1) on the basis of X-ray crystallography [2]. Due to the unique structure of these compounds and their potent activities, much research has focused on their biological aspects [3, 4]. These naturally occurring fish toxins are the only OP compounds that contains a P=O(S) moiety like that found in insecticides [5] and they do not have any good leaving groups. Another interesting feature of these compounds is the presence of free oximino functions, which were not found in the earlier reported

toxic OP compounds. The non availability of a P=O(S) analogue of these naturally occurring fish toxins [1] from the natural sources prompted us to develop a general synthetic method for the preparation of these compounds and their analogues for complete toxicological and pharmacological studies. In continuation of our ongoing research on the synthesis of new biologically active compounds, the possibility of synthesizing new analogues of phosphorohydrazido oximes was explored and recently, we have reported a method for the synthesis of various such derivatives [6-8]. Herein, we report a facile, cheap, extremely rapid and high-yielding procedure for the synthesis of *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oximes **5** from diacetyl-monoxime and *N,N*-dialkylamino-*O*-alkylphosphorohydrazides. To the best of our knowledge there are no reports in the literature describing the synthesis of these compounds.

Result and Discussion

Retrosynthetic analysis of the target compounds suggested that they could be synthesized from the corresponding phosphorohydrazides and butane-2,3-dione monoxime. We have thus followed the sequence shown in Scheme 1 to obtain the *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazidooximes **5a-j**.

Scheme 1.



In order to follow the proposed synthetic plan for the synthesis of target compounds, the intermediates **1-3** were prepared following literature procedures [9, 10]. After the synthesis of the various *N,N*-dialkylamino-*O*-alkyl-phosphorohydrazides **3** we optimized the reaction conditions for the synthesis of the target compounds **5**. In this regard, we initially performed as a model the reaction of diethylamino-*O*-butyl phosphorohydrazide with butane-2,3-dione monoxime in the presence of various dehydrating reagents, while varying reaction times and temperatures. The efficiency of various condensing agents such as Al₂O₃ (neutral, acidic, basic), SiO₂, ZnCl₂, H₃PO₃, KF-SiO₂, POCl₃, PTSA, BiCl₃, DCC, V₂O₅-SiO₂ were studied using different molar ratios. The results of these experiments are summarized in Table 1.

The results shown in Table 1 reveal that in comparison to other condensation reagents, the use of silica gave the best results. Next, to study the effect of solvent in the model reaction, various solvents

like THF, dioxane, hexane, diethyl ether, benzene, DCM, chloroform and CCl₄ were used and it was observed that benzene afforded the best results. During this study we observed that that yield of **5** was affected by changing the nature of solvent. It was also revealed that the use of DCM, chloroform and CCl₄ gave more or less similar yields of **5** (35-40%). However, when the reaction time was increased the isolation of products became difficult due to formation of some unidentified side products and unreacted starting materials. Diethyl ether and hexane were found to be poor solvents due to the limited solubility of the reactants in both the solvents, even under reflux conditions.

Table 1. Condensation agent optimization for the synthesis of compounds **5**^a.

Entry	Dehydrating agent	Solvent	Molar ratio of compound 3:4: dehydrating agents	Conversion (%)
1	Al ₂ O ₃ (neutral)	benzene	1:1:1	32
2	Al ₂ O ₃ (basic)	benzene	1:1:1	18
3	Al ₂ O ₃ (acidic)	benzene	1:1:1	42
4	H ₃ PO ₃	benzene	1:1:0.5	17
5	ZnCl ₂	benzene	1:1:1	19
6	DCC	benzene	1:1:2	15
7	PTSA	benzene	1:1:1	45
8	V ₂ O ₅ -SiO ₂	benzene	1:1:1	10
9	BiCl ₃	benzene	1:1:1	15
10	POCl ₃	benzene	1:1:0.5	8
11	ZnCl ₂	benzene	1:1:1	29
12	SiO ₂	benzene	1:1:1	52
13	SiO ₂	benzene	1:1:4	78
14	SiO ₂	benzene	1:1:6	78

10. All the reactions were performed for a constant time (3 hr) and temperature (100 °C) and reactions were monitored by ³¹P-NMR in C₆D₆ at 162 MHz.

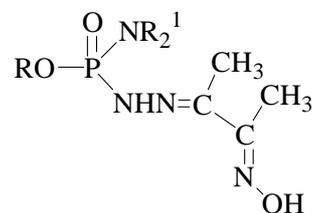
After optimization of reaction conditions, various *N,N*-dialkylamino-*O*-alkyl phosphorohydrazides were condensed with diacetylmonoxime in presence of activated silica in benzene, to give *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene) phosphorohydrazido oximes **5a-j** in excellent yield (Table 2).

Conclusions

In summary, we have described a general and efficient method for the synthesis of structurally complex and diverse *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oximes. It was found that procedure offers several advantages, including the possibility of obtaining pure products in high yields without the use of column chromatography, operational simplicity and cleaner reactions, which makes it a useful and attractive process for the synthesis of these compounds.

The assignment of the configuration and the detailed biological activity is under progress and will be reported in due course.

Table 2. Physical data of the newly synthesized compounds **5^a**.



Entry	R	R ¹	Reaction time (h)	³¹ P-NMR ^b	m. p. (°C)	Yield ^c (%)
5a	OC ₄ H ₉	C ₂ H ₅	2.8	9.95	103	78
5b	OC ₄ H ₉	C ₃ H ₇	2.9	10.11	112	75
5c	OC ₄ H ₉	ⁱ C ₃ H ₇	3.0	10.14	105	83
5d	OC ₄ H ₉	C ₄ H ₉	3.0	10.27	118	86
5e	OC ₄ H ₉	ⁱ C ₄ H ₉	3.2	9.88	121	79
5f	OC ₃ H ₇	C ₂ H ₅	2.7	10.15	110	72
5g	OC ₃ H ₇	C ₃ H ₇	2.8	10.04	120	73
5h	OC ₃ H ₇	ⁱ C ₃ H ₇	3.0	10.03	123	83
5i	OC ₃ H ₇	C ₄ H ₉	3.0	9.98	113	69
5j	OC ₃ H ₇	ⁱ C ₄ H ₉	3.0	10.02	130	81

a) All the reactions were performed in benzene under reflux conditions; b) ³¹P-NMR data were recorded at 162 MHz using either CDCl₃ or DMSO-d₆ as solvents; c) isolated yields

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Experimental

General

¹H-, ³¹P- and ¹³C-NMR spectra were recorded in CDCl₃ or DMSO-d₆ solutions on a Bruker AVANCE 400 NMR spectrometer operating at 400, 162 and 100 MHz, respectively. LCMS analysis (EI, 70V) were performed on a Hewlett-Packard HP 5971 instrument. IR spectra were recorded on a Bruker model Tensor 27 FT-IR spectrometer as KBr pellets.

General procedure for the preparation of *N,N*-dialkylamino-*O*-alkyl-2-(1-methyl-2-oxopropylidene)-phosphorohydrazido oximes: *N,N*-diethylamino-*O*-butyl-2-(1-methyl-2-oxopropylidene) phosphorohydrazido oxime (**5a**):

A mixture of butane-2,3-dione monoxime (1 g, 0.01 mol) and activated silica gel (2 g) was placed in a two necked round bottom flask containing benzene (20 mL). *N,N*-diethylamino-*O*-butyl phosphorohydrazide (2.23 g, 0.01 mol) diluted in benzene (20 mL) was slowly added at room temperature with efficient stirring and the resulting mixture was then refluxed for 3h. The reaction was monitored by ^{31}P -NMR until the *N,N*-diethylamino-*O*-alkyl phosphorohydrazide signal disappeared. The reaction mixture was filtered through Buchner funnel and washed with benzene (2x10 mL). Filtrate and washes were combined and the solvent was removed by distillation. Finally, the desired crude product was triturated with dry ether gave a white crystalline powder which was recrystallized from ethanol-ether (7:3); m.p. = 103 °C; yield 78%; IR: 1024 (P-O-C), 1105 (P-N-N), 1197 (P=O), 1434 (C-N), 1609 (C=N), 2966 (C-H), 3220 (NH), 3450 (OH) cm^{-1} ; ^1H -NMR δ : 0.75 (t, J =7.89 Hz, 3H, CH_3), 0.90 (t, J =7.96 Hz, 6H, CH_3), 1.30 (m, J =7.53 Hz, 2H, CH_2), 1.55 (m, J =7.53 Hz, 2H, CH_2), 1.85 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 3.10 (m, J =6.09 Hz, 4H, CH_2), 3.98 (m, J =7.29 Hz, 2H, CH_2), 6.45 (d, $J_{\text{P-H}}$ =27.45 Hz, 1H, NH) 9.01 (s, 1H, OH); ^{13}C -NMR δ : 9.05 (CH_3), 13.59 (CH_3), 18.81 (CH_2), 26.16 (CH_3), 26.34 (CH_3), 32.31 (CH_2), 39.89 (CH_2), 65.44 (CH_2), 145.39 (C=N-NH), 156.16 (C=N-OH); MS (m/z): 307 (M+H) $^+$, 330 (M+Na) $^+$; Calcd. for $\text{C}_{12}\text{H}_{27}\text{N}_4\text{O}_3\text{P}$ (%): C 47.05, H 8.88, N 18.29; Found (%): C 47.08, H 8.90, N 18.28.

N,N-dipropylamino-*O*-butyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (**5b**): IR: 1013 (P-O-C), 1115 (P-N-N), 1204 (P=O), 1458 (C-N), 1607 (C=N), 2873 (C-H), 3217 (NH), 3352 (OH) cm^{-1} ; ^1H -NMR δ : 0.80 (t, J =7.69 Hz, 3H, CH_3), 1.05 (t, J =7.89 Hz, 6H, CH_3), 1.30 (m, J =7.53 Hz, 2H, CH_2), 1.45 (m, J =8.73 Hz, 4H, CH_2), 1.55 (m, J =7.53 Hz, 2H, CH_2), 1.90 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.85 (m, J =8.56 Hz, 4H, CH_2), 3.98 (m, J =7.30 Hz, 2H, CH_2), 6.47 (d, $J_{\text{P-H}}$ =27.28 Hz, 1H, NH), 9.10 (s, 1H, OH); ^{13}C -NMR δ : 9.39 (CH_3), 13.59 (CH_3), 19.01 (CH_2), 22.05 (CH_2), 26.10 (CH_3), 26.28 (CH_3), 32.31 (CH_2), 47.94 (CH_2), 65.72 (CH_2), 145.40 (C=N-NH), 156.95 (C=N-OH); MS (m/z): 335 (M+ H) $^+$, 357(M+Na) $^+$; Calcd. for $\text{C}_{14}\text{H}_{31}\text{N}_4\text{O}_3\text{P}$ (%): C 50.28, H 9.34, N 16.75; Found (%): C 50.26, H 9.38, N 16.75.

N,N-diisopropylamino-*O*-butyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (**5c**): IR: 1110 (P-O-C), 1132 (P-N-N), 1193 (P=O), 1450 (C-N), 1647 (C=N), 2852 (C-H), 3147 (NH), 3390 (OH) cm^{-1} ; ^1H -NMR δ : 0.75 (t, J =7.83 Hz, 3H, CH_3), 1.10 (d, J =8.45 Hz, 6H, CH_3), 1.30 (m, J =7.53 Hz, 2H, CH_2), 1.50 (m, J =8.25 Hz, 2H, CH), 1.55 (m, J =7.53 Hz, 2H, CH_2), 1.90 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 3.98 (m, J =7.30 Hz, 2H, CH_2), 6.70 (d, $J_{\text{P-H}}$ =30.77 Hz, 1H, NH), 8.30 (s, 1H, OH); ^{13}C -NMR δ : 9.38 (CH_3), 13.49 (CH_3), 15.45 (CH), 19.05 (CH_2), 26.09 (CH_3), 26.18 (CH_3), 32.31 (CH_2), 65.42 (CH_2), 148.66 (C=N-NH), 157.16 (C=N-OH); MS (m/z): 335 (M+ H) $^+$, 357(M+Na) $^+$; Calcd. for $\text{C}_{14}\text{H}_{31}\text{N}_4\text{O}_3\text{P}$ (%): C 50.28, H 9.34, N 16.75; Found (%): C 50.26, H 9.38, N 16.75.

N,N-dibutylamino-*O*-butyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (**5d**): IR: 1080 (P-O-C), 1173 (P-N-N), 1204 (P=O), 1437 (C-N), 1609 (C=N), 2858 (C-H), 3307 (NH), 3355

(OH) cm^{-1} ; $^1\text{H-NMR}$ δ : 0.85 (t, $J=7.54$ Hz, 6H, CH_3), 0.90 (t, $J=7.25$ Hz, 3H, CH_3), 1.15 (m, $J = 8.05$ Hz, 4H, CH_2), 1.35 (m, $J=8.15$ Hz, 2H, CH_2), 1.48 (m, $J=7.28$ Hz, 4H, CH_2), 1.78 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 3.05 (m, $J=8.95$ Hz, 4H, CH_2), 3.95 (m, $J=8.15$ Hz, 2H, CH_2), 6.85 (d, $J_{P-H}=27.73$ Hz, 1H, NH), 8.25 (s, 1H, OH); $^{13}\text{C-NMR}$ δ : 9.39 (CH_3), 13.59 (CH_3), 14.27 (CH_2), 18.81(CH_2), 22.05 (CH_2), 26.18 (CH_3), 26.38 (CH_3), 32.31(CH_2), 39.85 (CH_2), 65.72 (CH_2), 145.40 (C=N-NH), 156.95 (C=N-OH); MS (m/z): 363 (M+H) $^+$, 385 (M+Na) $^+$; Calcd. for $\text{C}_{16}\text{H}_{35}\text{N}_4\text{O}_3\text{P}$ (%): C 53.02, H 9.73, N 15.46; Found(%):C 53.04, H 9.75, N 15.47.

N,N-diisobutylamino-O-butyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (5e): IR: 1076 (P-O-C), 1148 (P-N-N), 1204 (P=O), 1452 (C-N), 1609 (C=N), 2856 (C-H), 3206 (NH), 3370 (OH) cm^{-1} ; $^1\text{H-NMR}$ δ : 0.85 (d, $J=7.83$ Hz, 12H, CH_3), 0.90 (t, $J=8.54$ Hz, 3H, CH_3), 1.15 (m, $J = 8.05$ Hz, 2H, CH_2), 1.35 (m, $J=8.05$ Hz, 2H, CH_2), 1.45 (m, $J=8.25$ Hz, 2H, CH), 1.85 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 2.75 (m, $J=8.25$ Hz, 4H, CH_2), 3.85 (m, $J=8.25$ Hz, 2H, CH_2), 6.50 (d, $J_{P-H}=29.05$ Hz, 1H, NH), 8.25 (s,1H, OH); $^{13}\text{C-NMR}$ δ : 9.45 (CH_3), 13.75 (CH_3), 18.83 (CH_2), 20.05 (CH), 26.18 (CH_3), 26.38 (CH_3), 32.46 (CH_2), 53.42 (CH_2), 65.72 (CH_2), 146.49 (C=N-NH), 156.05 (C=N-OH); MS (m/z): 363 (M+H) $^+$, 385 (M+Na) $^+$; Calcd. for $\text{C}_{16}\text{H}_{35}\text{N}_4\text{O}_3\text{P}$ (%): C 53.02, H 9.73, N 15.46; Found (%):C 53.04, H 9.75, N 15.47.

N,N-diethylamino-O-propyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (5f): IR: 1024 (P-O-C), 1105 (P-N-N), 1197 (P=O), 1434 (C-N), 1609 (C=N), 2966 (C-H), 3214 (NH), 3379 (OH) cm^{-1} ; $^1\text{H-NMR}$ δ : 0.80 (t, $J = 7.89$ Hz, 3H, CH_3), 1.05 (t, $J = 7.96$ Hz, 6H, CH_3), 1.55 (m, $J = 7.53$ Hz, 2H, CH_2), 1.85 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 3.10 (m, $J = 7.80$ Hz, 4H, CH_2), 3.98 (m, $J = 7.78$ Hz, 2H, CH_2), 6.45 (d, $J_{P-H} = 25.37$ Hz, 1H, NH), 8.25 (s, 1H, OH); $^{13}\text{C-NMR}$ δ : 9.05 (CH_3), 13.59 (CH_3), 18.81 (CH_2), 26.16 (CH_3), 26.34 (CH_3), 32.31 (CH_2), 39.89 (CH_2), 65.44 (CH_2), 145.39 (C=N-NH), 156.16 (C=N-OH); MS (m/z): 293(M+H) $^+$, 316(M+Na) $^+$; Calcd. for $\text{C}_{11}\text{H}_{25}\text{N}_4\text{O}_3\text{P}$ (%): C 45.20, H 8.62, N19.17; Found (%): C 45.22, H 8.65, N 19.20.

N,N-dipropylamino-O-propyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (5g): IR: 1013 (P-O-C), 1115 (P-N-N), 1204 (P=O), 1458 (C-N), 1607 (C=N), 2873 (C-H), 3217 (NH), 3352 (OH) cm^{-1} ; $^1\text{H-NMR}$ δ : 0.75 (t, $J=8.39$ Hz, 3H, CH_3), 1.12 (t, $J = 7.50$ Hz, 6H, CH_3), 1.45 (m, $J=8.25\text{Hz}$, 4H, CH_2), 1.55 (m, $J = 7.39$ Hz, 2H, CH_2), 1.90 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.85 (m, $J=8.25$ Hz, 4H, CH_2), 3.98 (m, $J = 7.30$ Hz, 2H, CH_2), 6.35 (d, $J_{P-H}=27.28$ Hz, 1H, NH), 9.10 (s, 1H, OH); $^{13}\text{C-NMR}$ δ : 9.39 (CH_3), 11.41 (CH_3), 22.05 (CH_2), 26.09 (CH_3), 26.18 (CH_3), 32.31 (CH_2), 47.94 (CH_2), 67.52 (CH_2), 145.40 (C=N-NH), 156.95 (C=N-OH); MS (m/z): 321 (M+H) $^+$, 343 (M+Na) $^+$; Calcd. for $\text{C}_{13}\text{H}_{29}\text{N}_4\text{O}_3\text{P}$ (%): C 48.74, H 9.12, N 17.49; Found (%): C 48.72, H 9.15, N 17.50.

N,N-diisopropylamino-O-propyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (5h): IR: 1074 (P-O-C), 1135 (P-N-N), 1205 (P=O), 1455 (C-N), 1653 (C=N), 2951 (C-H), 3247 (NH), 3360 (OH) cm^{-1} ; $^1\text{H-NMR}$ δ : 0.85 (t, $J=7.26$ Hz, 3H, CH_3), 1.05 (d, $J=8.45$ Hz, 12H, CH_3), 1.65 (m, $J = 7.53$ Hz, 2H, CH_2), 1.90 (s, 3H, CH_3), 2.05 (s, 3H, CH_3), 2.79 (m, $J=7.45$ Hz, 2H, CH), 3.98 (m, $J = 7.30$ Hz, 2H, CH_2), 6.55 (d, $J_{P-H}=30.77$, 1H, NH), 8.30 (s, 1H, OH); $^{13}\text{C-NMR}$ δ : 9.38 (CH_3), 13.49 (CH_3),

15.45 (CH), 19.01 (CH₂), 26.16 (CH₃), 26.34 (CH₃), 46.91 (CH₂), 148.66 (C=N-NH), 157.16 (C=N-OH); MS (m/z): 321 (M+ H)⁺, 343 (M+Na)⁺; Calcd. for C₁₃H₂₉N₄O₃P (%): C 48.74, H 9.12, N 17.49; Found (%): C 48.72, H 9.15, N 17.50.

N,N-dibutylamino-*O*-propyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (**5i**): IR: 1080 (P-O-C), 1173 (P-N-N), 1204 (P=O), 1437 (C-N), 1619 (C=N), 2951 (C-H), 3246 (NH), 3375 (OH) cm⁻¹; ¹H-NMR δ: 0.85 (t, *J*=7.39 Hz, 6H, CH₃), 0.90 (t, *J*=8.35 Hz, 3H, CH₃), 1.15 (m, *J* = 7.52 Hz, 4H, CH₂), 1.35 (m, *J*=8.75 Hz, 4H, CH₂), 1.65 (m, *J*=8.05 Hz, 2H, CH₂), 1.85(s, 3H, CH₃), 1.95 (s, 3H, CH₃), 3.05 (m, *J*=7.11 Hz, 4H, CH₂), 3.90 (m, *J*=8.27 Hz, 2H, CH₂), 6.50 (d, *J*_{P-H}=24.26 Hz, 1H, NH), 8.00 (s, 1H, OH); ¹³C-NMR δ: 9.73 (CH₃), 10.39 (CH₃), 14.09 (CH₂), 20.21 (CH₂), 26.10 (CH₃), 26.18 (CH₃), 31.06 (CH₂), 38.75 (CH₂), 66.03 (CH₂), 145.75 (C=N-NH), 156.67 (C=N-OH); MS (m/z): 363 (M+H)⁺, 385 (M+Na)⁺; Calcd. for C₁₅H₃₃N₄O₃P (%): C 51.71, H 9.55, N 16.08; Found (%):C 51.71, H 9.55, N 16.08.

N,N-diisobutylamino-*O*-propyl-2-(1-methyl-2-oxopropylidene)phosphorohydrazido oxime (**5j**): IR: 1053 (P-O-C), 1106 (P-N-N), 1202 (P=O), 1467 (C-N), 1615 (C=N), 2962 (C-H), 3206 (NH), 3370 (OH) cm⁻¹; ¹H-NMR δ: 0.85 (d, *J*=8.27 Hz, 12H, CH₃), 0.90 (t, *J*=8.54 Hz, 3H, CH₃), 1.65 (m, *J*=8.25 Hz, 2H, CH), 1.68 (m, *J*=8.01 Hz, 2H, CH₂), 1.95 (s, 3H, CH₃), 2.05 (s, 3H, CH₃), 2.95 (m, *J*=8.17 Hz, 4H, CH₂), 3.95 (m, *J*=7.28 Hz, 2H, CH₂), 6.50 (d, *J*_{P-H}=29.05 Hz, 1H, NH), 8.40 (s, 1H, OH); ¹³C-NMR δ: 9.45 (CH₃), 13.75 (CH₃), 18.83 (CH₂), 20.05 (CH), 26.18 (CH₃), 26.38 (CH₃), 32.46 (CH₂), 53.42 (CH₂), 65.72 (CH₂), 146.49 (C=N-NH), 156.05 (C=N-OH); MS (m/z): 349 (M+H)⁺, 371 (M+Na)⁺; Calcd. for C₁₅H₃₃N₄O₃P (%): C 51.71, H 9.55, N 16.08; Found (%):C 51.71, H 9.55, N 16.08.

References

1. Alam, M.; Sanduja, R.; Hossain, M. B.; Helm, D. V. *Gymnodinium breve* toxin. 1. Isolation and X-ray structure of O,O-dipropyl(E)-2-(1-methyl-2-oxopropylidene) phosphorohydrazidothiolate (E) Oxime from the red tide dinoflagellate *Gymnodinium breve*. *J. Am. Chem. Soc.* **1982**, *104*, 5232-5234.
2. Dinovi, M.; Trainor, D. A.; Nakanishi, K. The structure of PB-1, an unusual toxin isolated from the red tide dinoflagellate *Ptychodiscus brevis*. *Tetrahedron Lett.* **1983**, *24*, 855-858.
3. Husain, K.; Kaushik, M. P.; Gupta, A. K. Acute toxicity of synthetic *Gymnodinium breve* Toxin metabolite and its analogues in mice. *Ecotox. Environ. Safety* **1996**, *35*, 77-80.
4. (a) Koley, J.; Basak, A. K.; Das, M.; Sinha, S.; Dubey, S. N.; Majumder, P. K.; Gupta, A. K.; Das Gupta, S.; Koley, B. N. Effect of synthetic toxin of *Ptychodiscus brevis* on cardio-vascular and renal function. *Ind. J. Physiol. Allied Sci.* **1997**, *51*, 119-125; (b) Majumder, P. K.; Gupta, A. K.; Kaushik, M. P.; Deo Kumar; Dubey, S. N. Cardio-vascular effects of organophosphates toxin isolated from *Ptychodiscus brevis*. *Biomed. Environ. Sci.* **1997**, *10*, 85-92; (c) Majumder, P. K.; Gupta, A. K.; Deo Kumar; Kaushik, M. P.; Dubey, S.N. Mechanism of cardiotoxicity induced by a marine toxin isolated from *Ptychodiscus brevis*. *Ind. J. Expt. Bio.* **1997**, *35*, 650-654; (d) Majumder, P. K.; Gupta, A. K.; Deo Kumar; Dubey, S.N. Calcium modulatory properties of o,o-

- diphenylcyclooctylphosphoramidates from *Ptychodiscus brevis* in rat atria and smooth muscle. *Ind. J. Physiol. Pharmacol.* **1997**, *41*, 257-262.
5. Eto, M. *Organophosphorus Pesticides: Organic and Biological chemistry*; CRC Press: Cleveland, Ohio, USA; **1974**; Chapter 5.
 6. Kaushik, M. P.; Parashar, B. D.; Swamy, R.V. Synthesis of *Gymnodinium breve* toxin. *Ind. J. Chem.* **1988**, *27B*, 1150-1151.
 7. Kumar, R.; Gupta, A. K.; Kaushik, M. P. A Novel and Efficient Synthesis of N,N-Dialkylaminoisopropyl- and O-alkylisopropyl-2-(1-alkyl-2-oxopropylidene)phosphonohydrazido Oximes - Potential Marine Fish Toxin Analogues. Part 1. *Molecules* **2007**, *12*, 1334-1340.
 8. Kumar, R.; Gupta, A. K.; Kaushik, M. P. Novel and Efficient Synthesis of N,N-Dialkylaminoand O-alkylphenyl-2-(1-alkyl/phenyl-2-oxopropylidene) Phosphonohydrazido Oximes - Potential Marine Fish Toxin Analogues. Part 2. *Molecules* **2007**, *12*, 1632-1640.
 9. Kosolapoff, G.M.; Maier, L. *Organic phosphorus compounds*; Wiley-Interscience: New York, **1976**; Volume 7.
 10. Audrieth, L. F.; Gher, R.; Smith, W.C. Nitrogen compounds of the phosphoric and phosphonic acids. 1. Hydrazides of phenylphosphoric and diphenylphosphoric acids. *J. Org. Chem.* **1955**, *20*, 1288-1290.

Sample Availability: Contact the authors.