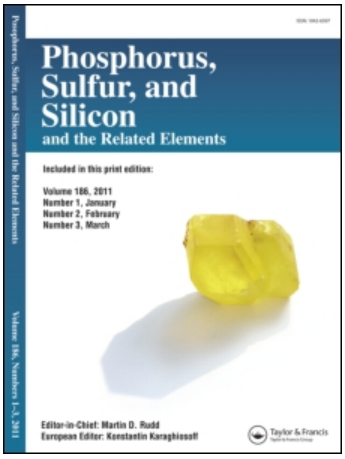

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Syntheses and Antimicrobial Activity of 2-Substituted-2,3-Dihydro-3-(4'-Bromophenyl)-1*H*-Naphth[1,2-*e*][1,3,2]Oxazaphosphorin 2-Oxides/Sulfides

D. Srinivasulu[a]; C. Devendranath Reddy[a]; C. Suresh Reddy[a]; Chad W. Brown[b]; Jacob D. Hager[b]; Michelle Means[b]; K. Darrell Berlin[b]
[a] Department of Chemistry, Sri Venkateswara University, Tirupati, India [b] Department of Chemistry, Oklahoma State University, Stillwater, OK, USA

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SYNTHESES AND ANTIMICROBIAL ACTIVITY OF 2-SUBSTITUTED-2,3-DIHYDRO-3-(4'-BROMOPHENYL)-1*H*-NAPHTH[1,2-*e*][1,3,2]OXAZAPHOSPHORIN 2-OXIDES/SULFIDES

D. SRINIVASULU[a], C. DEVENDRANATH REDDY[a], C. SURESH REDDY[a], CHAD W. BROWN[b], JACOB D. HAGER[b], MICHELLE MEANS[b] and K. DARRELL BERLIN[b]*

[a]*Department of Chemistry, Sri Venkateswara University, Tirupati, 517 502, India and* [b]*Department of Chemistry, Oklahoma State University, Stillwater, OK 74078 USA*

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The syntheses of the first examples of 2-aryloxy-2,3-dihydro-3-(4'-bromophenyl)-1*H*-naphth[1,2-*e*][1,3,2]-oxazahosphorin 2-oxides (**3a-g**) have been achieved from the reaction of equimolar quantities of 1-(4-bromoanilinomethyl)-2-naphthol (**1**) with various arylphosphorodichloridates in dry toluene in the presence of triethylamine at 50–55 °C. 2-Benzyloxy/aryloxy/arylthio/bis(2-chloroethyl)amino-2,3-dihydro-3-(4'-bromophenyl)-1*H*-naphth[1,2-*e*] [1,3,2]-oxazaphosphorin 2-sulfides (**3h-o**) have been synthesized through an intermediate monochloride, namely 2-chloro-2,3-dihydro-3-(4'-bromophenyl)-1*H*-naphth[1,2-*e*][1,3,2]oxazaphosphorin 2-sulfide (**2**). The structures of all products were confirmed by IR, ^{1}H, ^{13}C and ^{31}P NMR data as well as via mass spectral analysis. All compounds were screened for antibacterial activity against *Bacillus subtilis* and *Klebsiella pneumoniae* and for antifungal activity against *Aspergillus niger* and *Curvularia lunata*. A majority of the products exhibited significant activity in the assays.

Keywords: 2-Substituted-2,3-dihydro-3(4'-bromophenyl)-1*H*-naphth[1,2-*e*][1,3,2]oxazaphosphorin 2-oxides/sulfides; NMR analysis; mass spectral analysis; antimicrobial activities

INTRODUCTION

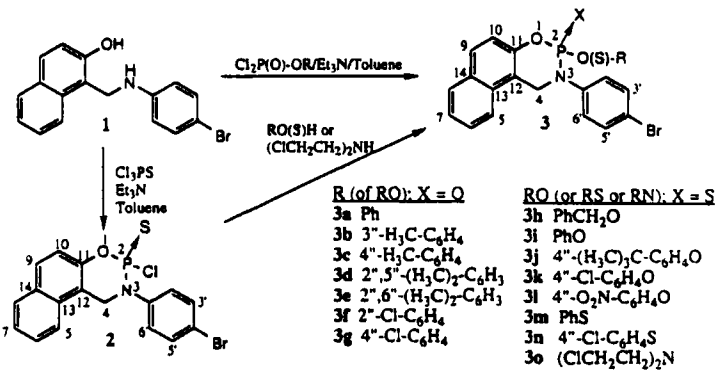
Naphthoxazaphosphorin 2-oxides/sulfides have exhibited good anticholinesterase activity[1] *in vitro*. Certain related *N*-phosphorylated nitrogen mustards, such as cyclophosphamide, are well known antineoplastic agents.[2]

* Corresponding Author.

The synthesis of naphth[1,2-*e*][1,3,2]oxazaphosphorin 2-oxides/sulfides (**3a-o**) (a very rare class of phosphorus-containing heterocycles), the corresponding structural characterization of these heterocycles by spectral studies (^{1}H, ^{13}C, ^{31}P NMR, and MS), and the antimicrobial activity thereof are reported in this paper as the first examples.

RESULTS AND DISCUSSION

Compounds **3a-g** were synthesized by the cyclocondensation of equimolar quantities of 1-(4-bromoanilinomethyl)-2-naphthol[3] (**1**) with arylphosphoro dichloridates[4] in the presence of triethylamine at 50–55 °C in anhydrous toluene over 5–6 h (Scheme I). Crude solids **3a-g** were obtained by filtration of the triethylamine hydrochloride, followed by evaporation of the filtrate. The residues were further purified by washing with water and recrystallization from ethanol and 2-propanol to afford colorless crystals or amorphous powders. In contrast, the syntheses of new naphthoxazaphosphorin 2-sulfides (**3h-o**) were achieved in a two-step route in which the intermediate **2** was formed but it proved far too hygroscopic to isolate or to characterize. To generate the P-sulfides, a reaction of **1** and thiophosphoryl chloride produced the key intermediate, 2-shloro-2,3-dihydro-3(4'-bromophenyl)-1*H*-naphth[1,2-*e*][1,3,2]oxazaphosphorin 2-sulfide (**2**). Treatment of **2** with benzyl alcohol/substituted phenols/thiophenols/bis(2-chloroethyl)amine led to the formation of title compounds **3h-o**. Physical and IR data,[5–11] as well as ^{1}H, ^{31}P, ^{13}C NMR, and mass spectral data, are given in Tables I, II, III, and IV.



SCHEME I

The proton NMR spectra of **3** showed complex multiplets[12] in the region δ 6.37–8.12 for aromatic protons of naphthoxazaphosphorin, *N*-phenyl, and 2-aryoxy moieties. Distinguishing between the proton signals of naphthoxazaphosphorin, *N*-phenyl, and 2-aryloxy moieties was not possible due to high signal density at 300 MHz.

Methylene (H-4) protons of the oxazaphosphorin ring moiety resonated as multiplets[13] at δ 4.56–5.56 as induced by coupling with phosphorus. A singlet was observed at δ 4.62 for methyleneoxy (-OCH_2) protons of the exocyclic benzyloxy moiety of **3h**. Both *N*-methylene and chloromethylene protons of the bis(2-chloroethyl)-amino moiety of **3o** appeared as complex multiplets in the regions of δ 3.98–4.01 and δ 4.41–4.54. The methyl protons of the 2-aryloxy moieties of **3b-3e** resonated as singlets in the region δ 2.19–2.24. The chemical shift of the methyl protons of the *tert*-butyl group in **3j** appeared as a singlet at δ 1.39.

Interpretation of the ^{13}C NMR data (Table III) was based, in part, upon an analysis of the intensities of non-protonated aromatic carbons and calculated chemical shift values. The low intensity chemical shifts at 146.3–148.2 ppm were assigned to the oxygen bearing carbon (C-11) of naphthoxaza-phoshorin 2-oxide. The quaternary carbons C-12, C-13, and C-14 showed low intensity signals at 113.7–116.4, 131.1–132.5, and 128.4–129.1 ppm, respectively, in the series. The high intensity singlet signals in the region 130.1–130.5, 121.6–124.6, 129.0–130.5, 129.1–130.2, 127.4–127.8, and 118.1–119.7 ppm were attributed to C-5, C-6, C-7, C-8, C-9, and C-10, respectively. Replacement of the phenoxy group by a bis(2-chloroethyl)amino group[12] caused a downfield chemical shift of ~ 2 ppm for C-12 and an upfield chemical shift of ~2 ppm for C-11. The bridged methylene protons resonated in the region 49.5–51.2 ppm for the target compounds but did not exhibit any observable coupling with phosphorus.

TABLE I Physical and IR data for **3a-3o**

Compd	*MF*	*MP(°C)*	*Yield (%)*	*Elemental Analyses*			*IR(cm^{-1})*					
				Found (Calcd-%)					*P-O-C_{arom}*		*P-N-C_{aliph}*	
				C	*H*	*N*	*P=O*	*P=S*	*P=O*	*O=C*	*N-C*	*P-N*
3a	$C_{23}H_{17}BrNO_3P$	149–150[a]	60	59.15 (59.25)	3.45 (3.67)	3.09 (3.00)	1302		986	1223	1071	775
3b	$C_{24}H_{19}BrNO_3P$	115–117[a]	58	59.85 (60.02)	3.79 (3.99)	2.76 (2.92)	1300		970	1225	1080	725
3c	$C_{24}H_{19}BrNO_3P$	110–112[a]	60	59.91 (60.02)	3.86 (3.99)	2.97 (2.92)	1305		975	1228	1080	730
3d	$C_{25}H_{21}BrNO_3P$	132–133[a]	52	60.81 (60.74)	4.39 (4.28)	2.73 (2.83)	1315		975	1235	1080	740
3e	$C_{25}H_{21}BrNO_3P$	142–143[a]	55	60.64 (60.74)	4.15 (4.28)	2.91 (2.83)	1302		973	1236	1045	735
3f	$C_{23}H_{16}BrClNO_3P$	136–137[a]	61	55.01 (55.17)	3.37 (3.22)	2.92 (2.80)	1290		970	1220	1075	730
3g	$C_{23}H_{16}BrClNO_3P$	133–134[a]	64	55.25 (55.17)	3.15 (3.22)	2.85 (2.80)	1295		975	1230	1078	735
3h	$C_{24}H_{19}BrNO_2PS$	181–182[b]	58	58.20 (58.08)	3.91 (3.86)	2.75 (2.82)		803	957	1206	1074	
3i	$C_{23}H_{17}BrNO_2PS$	178–179[b]	56	57.15	3.42	2.75		811	979	1228	1067	

Compd	MF	MP(°C)	Yield (%)	Elemental Analyses Found (Calcd-%)			IR(cm^{-1})				
									P-O-C_{arom}		P-N-C_{aliph}	
				C	H	N	P=O	P=S	P=O	O=C	N-C	P-N
				(57.27)	(3.55)	(2.90)						
3j	$C_{27}H_{25}BrNO_2PS$	175–177[b]	50	60.09	4.55	2.47		809	953	1220	1065	
				(60.23)	(4.68)	(2.60)						
3k	$C_{23}H_{16}BrClNO_2PS$	183–184[b]	55	53.28	3.00	3.58		811	957	1221	1067	
				(53.46)	(3.13)	(2.71)						
3l	$C_{23}H_{16}BrN_2O_4PS$	191–192[b]	52	52.45	3.15	5.45		815	952	1215	1099	
				(52.39)	(3.06)	(5.31)						
3m	$C_{23}H_{17}BrNOPS_2$	185–186[b]	57	55.28	3.55	2.85		811	943	1214	1082	
				(55.43)	(3.44)	(2.81)						
3n	$C_{23}H_{16}BrClNOPS_2$	187–189[b]	59	51.95	3.10	2.49		806	955	1216	1090	
				(51.85)	(3.03)	(2.63)						
3o	$C_{21}H_{20}BrCl_2N_2OPS$	181–182[b]	49	47.42	3.92	5.15		818	950	1206	1096	
				(47.57)	(3.80)	5.28)						

a. Recrystallized from ethanol.
b. Recrystallized from isopropyl alcohol.

TABLE II ^{1}H ($DCCl_3$/TMS/δ) and ^{31}P (85% H_3PO_4) NMR data (ppm) for **3a-3o**

Compd	*Ar-H*	*4-CH_2*	*R"-CH_3*	*^{13}P*
3a	7.10–7.35, 7.49–7.92 (m, 15 H)	5.06–5.31 (m, 2 H)		–10.20
3b	6.64–7.28, 7.45–7.92 (m, 14 H)	4.86–5.09 (m)	2.21 (s)	–12.19
3c	6.50–7.17, 7.55–7.97 (m, 14 H)	4.56–4.95 (m)	2.20 (s)	–13.43
3d	6.71–6.84, 7.36–7.65, 8.00–8.04 (m, 13 H)	5.28–5.34 (m)	2.19, 2.24 (s, 2"-CH_3, 5"-CH_3)	–5.14
3e	6.72–6.78, 7.22–7.35 (m, 13 H)	5.04–5.28 (m)	2.22 (s, 6 H, 2 CH_3)	–5.16
3f	6.86–7.45, 7.52–8.02 (m, 14 H0)	5.03–5.24 (m)		–12.26
3g	6.82–7.39, 7.53–7.98 (m, 14 H)	4.98–5.24 (m)		–14.70
3h[a]	6.41–6.53, 7.25–8.07 (m, 15 H)	5.03–5.42 (m)		+51.47
3i	6.37–6.42, 7.22–8.00 (m, 15H)	4.87–5.38 (m)		+52.86
3j	6.65–6.73, 7.22–7.85 (m, 14 H)	5.01–5.30 (m)	1.39 (s, 9 H)	+53.92
3k	6.51–6.54, 7.14–7.64, 7.90–8.04 (m, 14 H)	5.30–5.40 (m)		+58.85
3l	6.38–6.45, 7.20–8.03 (m, 14 H)	5.00–5.18 (m)		+65.43
3m	6.46–6.56, 7.20–8.01 (m, 15 H)	5.05–5.50 (m)		+85.74
3n	6.50–6.62, 7.35–8.12 (m, 14 H)	5.11–5.56 (m)		+86.23
3o[b]	6.40–6.43, 7.28–7.64, 7.82–8.01 (m, 10 H)	5.02–5.35 (m)		+55.92

a. OCH_2; δ 4.62.
b. $(CH_2\text{-}CH_2)_2Cl$; δ 3.98–4.01 and 4.41–4.54 (m, 8 H).

TABLE III ^{13}C NMR data for representative members of **3**[a] (ppm from TMS)

Carbons	*3a*	*3c*	*3e*	*3g*	*3j*	*3k*	*3m*	*3o*
C-4	50.9	51.2	49.8	51.1	50.2	51.0	51.1	49.5
C-5	130.2	130.5	130.5	130.1	130.3	130.2	130.2	130.3
C-6	121.6	124.6	122.8	122.7	122.5	122.7	122.2	124.0
C-7	129.8	130.5	129.9	129.2	129.7	129.3	129.4	129.0
C-8	129.1	130.2	129.6	129.7	130.1	129.6	129.8	129.5
C-9	127.7	127.5	127.8	127.4	127.7	127.4	127.4	127.7
C-10	119.1	118.9	118.1	119.7	119.2	119.7	119.4	119.0
C-11	148.0	147.9	148.1	148.0	148.2	148.0	148.0	146.3
C-12	114.2	113.9	114.1	113.7	114.2	113.8	114.2	116.4

Carbons	*3a*	*3c*	*3e*	*3g*	*3j*	*3k*	*3m*	*3o*
C-13	132.5	131.1	132.1	131.9	132.3	131.9	132.5	132.0
C-14	129.1	128.4	128.5	128.6	129.0	128.6	128.9	128.6
C-1′	148.2	147.9	148.1	148.3	148.1	148.3	148.3	147.3
C-2′,6′	119.1	119.6	119.2	119.2	119.4	119.4	119.6	118.9
C-3′,4′	132.5	131.3	132.1	132.2	131.9	132.2	131.1	132.7
C-4′	113.8	113.9	114.2	114.1	114.0	114.1	114.1	114.4
C-1″	150.3	149.1	152.5	152.7	151.9	152.7	131.1	51.8
C-2″	120.2	113.9	122.8	115.8	115.6	115.8	128.7	39.1
C-3″	129.8	130.5	129.6	129.7	126.8	129.6	128.8	
C-4″	126.2	130.2	120.8	127.2	142.9	130.2	125.5	
C-5″	129.8	130.5	136.7	129.7	126.8	129.6	128.8	
C-6″	120.2	113.9	117.3	115.8	115.6	115.8	128.8	
R″-CH_3		20.3	20.6		13.7 (H_3C)			
					36.1 (*t*-C)			

[a]Not recorded for **3b, 3d, 3f, 3h, 3i, 3l**, and **3n**.

The nitrogen bearing carbon C-1′ appeared as a singlet in the range of 147.3–148.3 ppm. The other protonated carbons, C-2′/C-6′ and C-3′/C-5″ resonated in the region 118.9–119.6 ppm and 131.3–132.7 ppm, respectively, with high intensity. The bromine bearing carbon (C-4′) signal appeared as a low intensity singlet at 113.8–114.4 ppm.

The signal for C-1″ of the aryloxy ring resonated at 149.1–152.7 ppm in most compounds except for the signal for the same C-1″ in **3m** which appeared at 131.1 ppm, possibly due to influence by the unsubstituted thiophenoxy ring. The chemical shifts of C-1″ and C-2″ of **3o** appeared at 51.8 ppm and 39.1 ppm, respectively, apparently as the result of the proximity of the bis(2-chloroethyl)amino moiety. In general, the carbon signals of C-2″/C-6″ and C-3″/C-5″ signals resonated in the expected regions (see Table III). However, a large upfield shift noted for the carbon of the methyl group attached to C-2″/C-6″ in **3e** is likely the result of a γ-interaction with the non-bonded electrons of the exocyclic oxygen[14–16] atom which, in turn, may force the methyl carbons out of the plane of the aromatic ring.

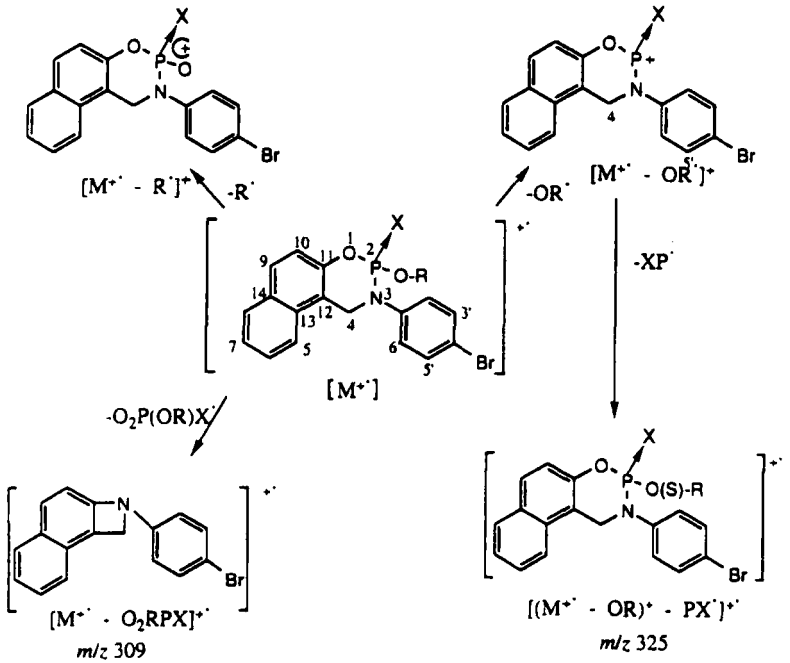
The downfield ^{13}C NMR signal at 142.9 ppm in **3j** was attributed to the attached aryl carbon of the phenyl group. Compounds **3k** and **3m** showed a similar signal for C-4″ at 130.2 and 125.5 ppm, respectively. The methyl carbons attached to C-4″ and C-2″/C-6″ appeared at 20.3 and 20.6 ppm in **3c** and **3e**, respectively. Interestingly, the quaternary carbon of the *t*-butyl carbon at C-4′ resonated at 36.1 ppm, and the methyl carbons of the *t*-butyl group appeared as a high intensity singlet at 13.7 ppm in **3j**.

Resonances for ^{31}P signals (Table II) in the NMR spectra were observed in the range of −5.14 to −14.70 ppm for **3a-3g**. Heterocycles **3h-3o** exhibited ^{31}P NMR signals somewhat downfield and in the region of +51.47 to +86.23 ppm. The difference in the ^{31}P NMR chemical shift of naphthoxazaphosphorin 2-oxides (**3a-3g**) and naphthoxazaphosphorin 2-sulfides (**3h-3o**) may be due, in part, to the difference in the electronegative differences between oxygen and sulfur as well as subtle steric effects imposed by substituents.

The EI mass spectra of **3** (Table IV) exhibited $M^{+\cdot}$, along with isotopic peaks in the expected ratio whichconfirmed the presence of bromine, sulfur, and chlorine atoms. Other characteristic major daughter ions are observed[18] at $(M^+\text{-}R)^{+\cdot}$, $(M^+ - OR)^{+\cdot}$, $(M^{+\cdot} - O_2\ RPX)^{+\cdot}$, and $[(M^+ - OR)^+ - PX]^{+\cdot}$ (Scheme II). The appearance of these ions support the proposed structures for member of **3**.

TABLE IV Mass spectral data for representative members of **3**

Compd	*m/z (relative intensity)*
3a	467 [($M^{+\cdot}$ + 2), 86], 465 ($M^{+\cdot}$, 87), 3.88 (12), 372 (58), 325 (14), 309 (100) 230 (44), 167 (28) 128 (45), 115 (13), 77 (53)
3e	495 [($M^{+\cdot}$ + 2), 100], 493 ($M^{+\cdot}$, 100), 388 (18), 372 (85), 325 (90), 309 (28), 230 (14), 195 (13) 128 (43), 105 (16), 77 (44)
3f	503 [($M^{+\cdot}$ + 4), 30], 501 [($M^{+\cdot}$ + 2), 100], 499 ($M^{+\cdot}$, 100), 419 (18), 388 (24), 372 (56), 325 (68), 309 (14), 230 (18), 195 (39), 128 (41)
3h	499 [($M^{+\cdot}$ + 4), 2], 497 [($M^{+\cdot}$ + 2), 35], 495 ($M^{+\cdot}$, 38), 419 (22), 405 (4), 387 (6), 325 (16), 309 (11), 230 (8), 189 (100), 154 (18), 126 (20), 128 (14), 108 (1)
3k	521 [($M^{+\cdot}$ + 6), 2], 519 [($M^{+\cdot}$ + 4), 5], 517 [($M^{+\cdot}$ + 2), 20], 515 [($M^{+\cdot}$, 10), 482 (20), 404 (3), 388 (5), 325 (6), 309 (8), 230 (5), 209 (100), 174 (22), 152 (8), 126 (16)
3o	536 [($M^{+\cdot}$ + 8), 2], 534 [($M^{+\cdot}$ + 6), 6], 532 [($M^{+\cdot}$ + 4), 5], 530 [($M^{+\cdot}$ + 2), 26], 528 ($M^{+\cdot}$, 18), 513 (18), 464 (15), 388 (11), 373 (19), 368 (6), 342 (14), 325 (23), 309 (100), 230 (10), 200 (33), 153 (20), 128 (33)



SCHEME II

ANTIMICROBIAL STUDIES

All the naphth[1,2-*e*]oxazaphosphorn 2-oxides/sulfides were tested for antibacterial activity on *Bacillus subtilis* and *Klebsiella pneumoniae* at concentrations of 250 and 500 ppm by using the Vincent method.[19] The compounds containing substituted chloro- and nitroaryloxy, as well as the arylthio groups, showed reasonable activity against these bacteria at the two concentrations (Table V). Antifungal activity was determined by using the Horsfall and Rich technique[20] on *Aspergillus niger* and *Curvularia lunata*. The best activity in the P→O series (**3a-3g**) was observed with **3f** and **3g** while in the P→S series **3l, 3m**, and **3o** proved most effective against *Bacillus subtilis* and *Klebsiella pneumonia*, particularly at the concentration of 500 ppm. Tetracycline was the standard employed for the study with these two bacteria and showed zones of inhibition of 30 mm and 25 mm at 100 ppm, respectively.

TABLE V Antimicrobial activity (zone of inhibition in mm) of **3a-3o**

Compd	*Bacillus Subtilus*		*Klebsiella pneumoniae*		*Aspergillus niger*		*Curvularia lunata*	
	250[a]	500[a]	250[a]	500[a]	250[a]	500[a]	250[a]	500[a]
3a	12	14	9	10	62	83	63	80
3b	-[b]	–	–	–	55	67	51	65
3c	–	–	–	–	72	84	64	78
3d	–	–	–	–	65	77	58	70
3e	–	–	–	–	58	65	55	68
3f	13	15	11	12	75	91	65	81
3g	14	16	10	12	75	86	71	88
3h	–	–	–	–	–	–	–	–
3i	11	14	9	13	60	72	68	53
3j	–	–	–	–	55	67	62	78
3k	15	17	12	15	72	85	78	91
3l	16	19	14	16	75	89	81	95
3m	15	20	13	17	74	92	79	88
3n	14	18	14	16	75	92	79	94
3o	18	22	17	20	80	94	85	96

a. Concentration in ppm.
b. The hyphen "-" indicates inactivity.

Griseofulvin was the reference compound in the investigation with the two fungi and, at 50 ppm, exhibited 100% inhibition of growth of *Aspergillus niger* and *Curvularia lunata*. In the series of **3a-3g** and at 250 ppm, **3f** and **3g** were again the most effective against the latter two bacteria while in the series **3h-3o** both **3l** and **3o** exhibited the highest inhibition of growth at 250 ppm.

In summary, it is clear that the activity of agents **3a-3o** in terms of inhibition of growth of the four bacteria is modest. Nevertheless, the unusual title compounds may well possess useful properties as antibacterial agents against other bacteria or for insecticidal purposes, and thus such heterocycles deserve additional evaluation.

CONCLUSIONS

We have developed a simple method to obtain several of the first members of the title compounds from available bifunctional phenols/amines. The

structures of the target products were confirmed by elemental and spectral characterization. In addition, preliminary antimicrobial activity for this new family of organophosphorus heterocycles was modestly effective as growth inhibitors of the bacteria *Bacillus subtilis* and *Klebsiella pneumoniae* and against the fungi *Aspergillus niger* and *Curvularia lunata*.

EXPERIMENTAL

Melting points were obtained on a Mel-Temp apparatus and were not corrected. Elemental analyses were recorded by RSIC, Central Drug Research Institute, Lucknow India. IR spectra were recorded in KBr pellets on a Perkin-Elmer 1430 unit. All ^{1}H, ^{13}C, and ^{31}P NMR spectra were taken on a Varian Gemini 300 MHz NMR spectrometer operating at 299.9 MHz for ^{1}H, 75.43 MHz for ^{13}C, and 121.7 MHz for ^{31}P. All NMR data were observed on solutions of $DCCl_3$ or DMSO-d_6 and were referenced from TMS (^{1}H and ^{13}C, δ or ppm). All ^{31}P NMR data were taken on similar solutions and referenced to 85% H_3PO_4 (^{31}P, ppm). Mass spectral data (EI) were collected on a JEOL JMSD-300 instrument at 70 eV with a direct inlet system. General procedures for the preparations of members of **3a-3g** and **3h-3o** are illustrated with the syntheses of **3a** and **3k**, respectively. Intermediate **2** could not be isolated since it was extremely moisture sensitive and had to be utilized in situ as formed without exposure to the atmosphere.

2-Phenoxy-2,3-dihydro-3-(4′-bromophenyl)-1H-naphth[1,2-*e*] [1,3,2]oxazaphosphorin 2-Oxide (3a)

A solution of phenylphosphorodichloridate (0.63 g, 0.003 mol) in dry toluene (20 mL) was added dropwise (20 min) to a cooled (0 °C) and stirred solution of 1-(4-bromoanilinomethyl)-2-naphthol (**1**, 1.06 g, 0.003 mol) and triethylamine (0.60 g, 0.006 mol) in dry toluene (60 mL). After completion of the addition, the temperature of the reaction mixture was slowly raised to room temperature and was stirred for 2 h. The reaction mixture was then heated to 50–55 °C for another 3 h with stirring. Monitoring of the reaction was accomplished by TLC analysis. The solid triethylamine hydrochloride was filtered off, and the filtrate was evaporated under

reduced pressure. The resulting gummy residue was washed with water, dried, and washed with cold 2-propanol. A white amorphous solid obtained was recrystallized (ethanol) to afford **3a**; yield 0.84 g (60%), mp 149–150 °C. Physical and spectral data for **3a-o** are given in Tables I-IV.

2-(4″-Chlorophenoxy)-2,3-dihydro-3-(4′-bromophenyl)-1*H*-naphth[1,2-*e*][1,3,2]oxazaphosphorin 2-Sulfide (3k)

A solution of thiophosphoryl chloride (0.51 g, 0.003 mol) in dry toluene (20 mL) was added dropwise to a cooled (0 °C) and stirred solution of 1-(4-bromoanilinomethyl)-2-naphthol (**1**, 1.06 g, 0.003 mol) and triethylamine (0.60 g, 0.006 mol) in dry toluene (20 mL). After the addition, the temperature of the reaction mixture was slowly raised to room temperature and was maintained there for 2 h. Stirring was continued for another 3 h at 40–50 °C. Formation of the intermediate, 2-chloro-2,3-dihydro-3-(4′-bromophenyl)-1*H*-naphth[1,2-*e*][1,3,2]oxazaphosphorin 2-sulfide (**2**) was monitored by TLC.

To a cooled (0–5 °C) solution of **2** (not purified) was added dropwise a solution of 4-chlorophenol (0.38 g, 0.003 mol) and bis(2-chloroethyl)-amine (0.4 g, 0.003 mol) in dry toluene (20 mL). After the addition, the temperature of the reaction mixure was raised slowly to 40–50 °C, and stirring was continued for another 3 h. TLC analysis was utilized to determine the completion of the reaction. Solid bis(2-chloroethyl)-amine hydrochloride was filtered off, and the solvent was evaporated under reduced pressure. The residue was washed with water and cold 2-propanol. Recrystallization of the solid (2-propanol) afforded **3k** (0.85 g, 55%), mp 183–184 °C.

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