Synthesis and antimicrobial activity of some oxazaphosphinine oxides

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Abstract

A new family of phosphorus heterocycle, namely 2-substituted 3-[4-(2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl)phenyl]-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphinin-2-oxides (**5a–j**) has been synthesized by the condensation of 2-[[4-(2-hydroxy-benzylamino)-phenylamino]methyl]phenol (**1**) with phosphorus oxychloride in presence of triethylamine in dry tetrahydrofuran, followed by the reaction with various phenols **3a–j**. Alternatively, some of these compounds **5a-e** were prepared by the cyclocondensation of **1** with aryl phosphorodichloridates **4a–e**. All title compounds were characterized by elemental and spectral analyses. Their antimicrobial activity was also evaluated.

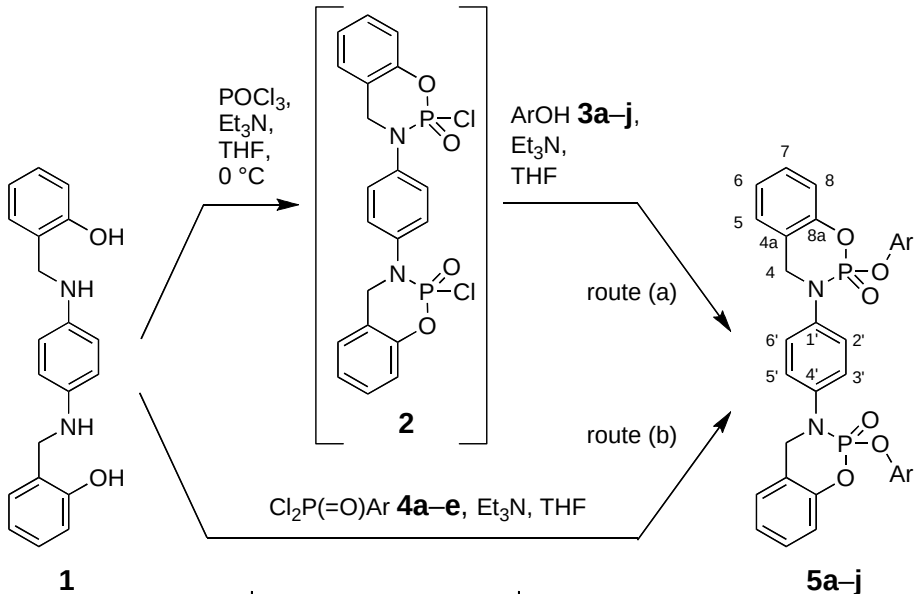
Keywords: Oxazaphosphinine, arylphosphorodichloridates, antimicrobial analysis, spectral analysis

Introduction

Organophosphorus heterocycles containing O and N in a six-membered ring have gained much attention ever since cyclophosphamide was discovered as anti-cancer drug.[1] Compounds of this class also have high anti-tumor activity,[2–5] significant bioactivity,[6] and outstanding medicinal properties.[7] The significant activity of all these compounds was accredited to the presence of six-membered heterocyclic rings. In our present research, synthesis of compounds containing two such rings was accomplished successfully. All compounds were characterized by elemental, IR, ^{1}H, ^{13}C and ^{31}P NMR and mass spectral analysis. Their antimicrobial activity was also evaluated.

Results and Discussion

Cyclocondensation of 2-[[4-(2-hydroxybenzylamino)phenylamino]methyl]-phenol (**1**) with phosphorus oxychloride in presence of triethylamine in dry tetrahydrofuran at 40–50 °C afforded 2-chloro-3[4-(2-chloro-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinine-2-oxide (**2**), which upon subsequent reaction with various phenols **3a**–**j** gave 3-[4-(2-aryloxy-2-oxo-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphinine-3-yl)phenyl]-2-aryloxy-3,4-dihydrobenzo-[*e*][1,3,2]oxazaphosphinine-2-oxides (**5a**–**j**) in good yields. Some products **5** were prepared by condensation of **1** with aryl phosphorodichloridates[8] **4a**–**e** in the presence of triethylamine in dry THF. The yields of the products obtained by both routes are comparable. Direct condensation of compound **1** with aryl phosphorodichoridates (**4a-e**) afforded good yields more conveniently than the former method because compound **2** is highly moisture sensitive and difficult to handle. All compounds were purified by recrystallizing from 2-propanol and were characterized by elemental, IR, ^{1}H, ^{13}C, ^{31}P NMR, and partly by mass spectral analyses.



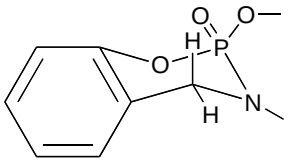
3,4,5	Ar
a	Ph
b	2-ClC_6H_4
c	4-ClC_6H_4
d	4-$O_2NC_6H_4$
e	4-MeC_6H_4

3,5	Ar
f	2-MeC_6H_4
g	3-MeC_6H_4
h	3-Me,4-ClC_6H_3
i	2,4-$Cl_2C_6H_3$
j	2,6-$Me_2C_6H_3$

Scheme 1

All compounds **5a-j** exhibit characteristic IR absorption bands in the regions 1196–1231, 1109–1131, and 908–921 cm^{-1} indicative of (P=O),[9-11] (C-O), and (P–O),[12,13] respectively. ^{1}H

NMR spectra of compounds **5a–j** exhibit multiplets in the range δ 6.19–8.17 for aromatic protons. Methylene protons resonate as multiplets at δ 4.41–5.09 indicating their nonequivalence[14] and coupling with phosphorus in the six-membered chair-like conformation of the benzoxazaphosphinine system.



In the ^{13}C NMR spectra of compounds **5a–j**, the oxygen-bearing C-8a exhibits signals in the range of δ 149.5–153.9. The signal in the region δ 129.2–129.7 is assigned to C-4a. Signals in the ranges of δ 128.4–129.0 and 123.3–124.4 are assigned to C-5 and C-6, respectively. The two signals exhibited at δ 132.3–133.0 and 115.8–118.9 are attributed to C-1',4' and C-2',3',5',6', respectively. Methylene C-4 appears as a doublet in the range δ 45.3–46.3 ($^2J_{PC}$ = 124.78–132.43 Hz). ^{31}P NMR chemical shift values[15] of these compounds appears within the range of δ 1.23–6.84. The above data suggest that the two benzoxazaphosphonine rings are present in the same chemical and magnetic environment.

Antimicrobial activity

Compounds **5a-j** were screened for their antibacterial activity[16,17] against gram-positive *Staphylococcus aureus* and gram-negative *Klebsiella pneumoniae* by the disc-fusion method in nutrient agar medium at two concentrations (200, 400 ppm) in DMF. These solutions were added to each filter disc, and the plates were incubated at 35 °C and examined for zone of inhibition around each disc after 24 h. Results were compared with the activity of the standard antibiotic Penicillin. Antifungal activities were evaluated against *Pellicularia solmanicolor* and *Macrophomina phaseolina* at two concentrations[18] (200, 400 ppm) using Griseofulvin as reference compound. Fungal cultures were grown on potato dextrose broth at 25 °C and spore suspension was adjusted to 10^5 spore/mL. All compounds exhibited antimicrobial activity comparable with that of reference compounds. Some of the compounds showed high acivity againist both the bacteria and fungi.

Table 1. Antibacterial and antifungal activities of **5a–j**

Compound	Zone of inhibition							
	Staphylococcus aureus		*Klebsiella pneumoniae*		*Pellicularia solamnicolor*		*Macrophomina phaseolina*	
	200[a]	400[a]	200[a]	400[a]	200[a]	400[a]	200[a]	400[a]
5a	23	46	21	39	21	47	20	46
5b	21	43	24	45	20	44	18	42
5c	19	37	20	41	22	50	24	50
5d	17	36	22	43	18	42	16	39
5e	20	42	20	40	24	51	25	48
5f	15	31	17	36	19	44	20	45
5g	21	42	16	34	21	46	17	40
5h	25	48	22	43	22	49	23	50
5i	19	38	16	36	20	48	19	45
5j	21	41	19	40	19	43	17	41
Penicillin[b]	22	41	24	46				
Griseofulvin[b]					23	44	24	47

[a]In DMF, concentration in ppm. [b]Standard reference.

Experimental Section

General Procedures. Melting points were determined in open capillary tubes on a Mel-Temp apparatus. IR spectra were recorded on a Perkin Elmer 1000 unit. The ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on Varian Gemini 300 and Varian AMX 400 NMR spectrometers operating at 300 or 400 MHz (^{1}H), 75.46 or 100.57 MHz (^{13}C) and 121.7 MHz (^{31}P). Mass spectra were recorded by Fast Atom Bombardment mass spectrometer. All compounds were dissolved in DMSO-d_6, chemical shifts are referenced to TMS (^{1}H, ^{13}C) and 85% H_3PO_4 (^{31}P). Microanalytical data were obtained from Central Drug Research Institute, Lucknow, India.

3-[4-(2-Phenoxy-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl)-phenyl]-2-phenoxy-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphinin-2-oxide (5a). Typical procedure

(a) To a stirred solution of 2-[[4-(2-hydroxybenzylamino)phenylamino]methyl]phenol (**1,** 1.65 g, 5 mmol) in dry THF (25 mL) was added dropwise phosphorus oxychloride (0.932 g, 10 mmol) in dry THF (10 mL) in the presence of triethylamine (2.02 g, 20 mmol) at 0 °C. After addition, the temperature was slowly raised to 50–60 °C; the progress of the reaction was monitored by TLC. Triethylamine hydrochloride was sucked off. To the filtrate was added freshly distilled phenol (**3a**, 0.47 g, 5 mmol) in dry THF (15 mL) and triethylamine (1.01 g, 10 mmol), and the progress of the reaction was monitored by TLC. Triethylamine hydrochloride was filtered off, the solvent

was removed under reduced pressure. The crude product was recrystallized from 2-propanol to get colorless crystals **5a** (1.93 g, 65%).

(b) To a stirred solution of **1 (**1.65 g, 5 mmol) in dry THF (25 mL) was added dropwise phenyl phosphorodichloridate (**4a**, 2.1 g, 10 mmol) in dry THF (15 mL) in the presence of triethylamine (2.02 g, 20 mmol) at 0 °C. After addition, the temperature was maintained between 50–55 °C, and the progress of the reaction was monitored by TLC. The crude product was recrystallized from 2-propanol to yield **5a** (2.02 g, 68%).

5a. Mp 120–122 °C. IR (KBr): $\tilde{\nu}$ 1226 (P=O), 1128 (O–C), 916 (P–O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 6.70–7.81 (m, 22H), 4.50–4.70 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.4 (d, J_{PC} = 129.30 Hz, C-4), 129.2 (C-4a), 128.7 (C-5), 124.3 (C-5), 127.9 (C-7), 123.9 (C-8), 149.5 (C-8a), 132.6 (C-1', C-4'), 118.6 (C-2', C- 3', C-5',C-6'), 157.4 (1-C_{Ar}), 114.9 (2-C_{Ar}), 128.1 (3-C_{Ar}), 130.4 (4-C_{Ar}), 128.1 (5-C_{Ar}), 114.9 (6-C_{Ar}). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 2.98. FAB-MS: *m*/*z* (%) 596 (8, $M^{+\bullet}$), 508 (27), 504 (19), 456 (21), 368 (100), 276 (9), 248 (35). Anal. calcd. for $C_{32}H_{26}N_2O_6P_2$: C, 64.43; H, 4.39; N, 4.69. Found: C, 64.52; H, 4.46; N, 4.47.

5b-e were prepared by the above two procedures, **5f–j** were prepared following route (a).

3-[4-[2-(2-Chlorophenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl]-phenyl]-2-(2-chlorophenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5b). Route (b): Colorless crystals (2.12 g, 62%); mp 159–161 °C. IR (KBr): $\tilde{\nu}$ 1212 (P=O), 1118 (O-C), 913 (P-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 6.31–7.62 (m, 20H), 4.61–4.92 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 46.3 (d, J_{PC} = 131.12 Hz, C-4), 129.5 (C-4a), 128.7 (C-5), 123.3 (C-6), 127.9 (C-7), 119.3 (C-8), 151.4 (C-8a), 132.3 (C-1', C-4'), 116.3 (C-2', C-3', C-5', C-6'), 155.3 (1-C_{Ar}), 123.3 (2-C_{Ar}), 128.9 (3-C_{Ar}), 131.5 (4-C_{Ar}), 126.6 (5-C_{Ar}), 130.6 (6-C_{Ar}). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 1.23. Anal. calcd. for $C_{32}H_{24}Cl_2N_2O_6P_2$: C, 57.76; H, 3.64; N, 4.21. Found: C, 57.87; H, 3.69; N, 4.29.

3-[4-[2-(4-Chlorophenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl]-phenyl]-2-(4-chlorophenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5c). Route (b): Colorless crystals (1.93 g, 59%); mp 154–156 °C. IR (KBr): $\tilde{\nu}$ 1208 (P=O), 1131 (O-C), 917 (P-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 6.61–7.62 (m, 20H), 4.42–4.62 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.9 (d, J_{PC} = 130.19 Hz, C-4), 129.6 (C-4a), 128.6 (C-5'), 124.1 (C-6), 127.9 (C-7'), 121.3 (C-8'), 152.4 (C-8a), 132.5 (C-1', C-4'), 116.6 (C-2', C-3', C-5', C-6'), 154.6 (1-C_{Ar}), 130.9 (2-C_{Ar}), 128.9 (3-C_{Ar}), 135.6 (4-C_{Ar}), 128.9 (5-C_{Ar}), 130.9 (6-C_{Ar}). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 3.72. Anal. calcd. for $C_{32}H_{24}Cl_2N_2O_6P_2$: C, 57.76; H, 3.64; N, 4.21. Found: C, 57.84; H, 3.69; N, 4.30.

3-[4-[2-(4-Nitrophenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl]-phenyl]-2-(4-nitrophenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5d). Route (b): Pale yellow crystals (2.16 g, 61%); mp 139–142 °C. IR (KBr): $\tilde{\nu}$ 1196 (P=O), 1114 (O-C), 911 (P-O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 6.59–7.81 (m, 20H), 4.84–5.17 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.3 (d, J_{PC} = 133.11 Hz, C-4), 129.4 (C-4a), 128.4 (C-5), 124.2 (C-6), 128.1 (C-7), 122.9 (C-8), 152.1 (C-8a), 132.7 (C-1', C-4'), 115.4 (C-2', C-3', C-5', C-6'), 156.3 (1-C_{Ar}), 117.3 (2-C_{Ar}), 127.4 (3-C_{Ar}), 141.3 (4-C_{Ar}), 127.4 (5-C_{Ar}), 117.3 (6-C_{Ar}). ^{31}P

NMR (161.98 MHz, DMSO-d_6): δ 6.84. Anal. calcd. for $C_{32}H_{24}N_4O_{10}P_2$: C, 55.99; H, 3.52; N, 8.16. Found: C, 56.12; H, 3.68; N, 8.27.

3-[4-[2-(4-Methylphenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphos-phinin-3-yl]phenyl]-2-(4-methylphenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5e). Route (b): Colorless crystals (1.93 g, 60%); mp 161–163 °C. IR (KBr): $\tilde{\nu}$ 1212 (P=O), 1122 (O-C), 918 (P-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.14–7.77 (m, 26H), 4.75–4.94 (m, 4H), 1.92 (m, 4-H_{Ar}, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 46.1 (d, J_{PC} = 132.43 Hz, C-4), 129.7 (C-4a), 129.0 (C-5), 124.0 (C-6), 128.6 (C-7), 122.2 (C-8), 153.4 (C-8a), 133.0 (C-1', C-4'), 117.1 (C-2', C-3', C-5', C-6'), 156.3 (1-C_{Ar}), 119.3 (2-C_{Ar}), 128.9 (3-C_{Ar}), 139.4 (4-C_{Ar}), 128.9 (5-C_{Ar}), 130.0 (6-C_{Ar}), 20.9 (2C, 2CH_3). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 2.61. FAB-MS: *m*/*z* (%) 624 (12, $M^{+\bullet}$), 536 (19), 518 (21), 470 (33), 382 (100), 322 (31), 260 (13), 140 (36). Anal. calcd. for $C_{34}H_{30}N_2O_{12}P_2$: C, 65.39; H, 4.84; N, 4.49. Found: C, 65.47; H, 4.92; N, 4.57.

3-[4-[2-(2-Methylphenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphos-phinin-3-yl]phenyl]-2-(2-methylphenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5f). Route (a): Pale brown crystals (2.15 g, 67%); mp 144–146 °C. IR (KBr): $\tilde{\nu}$ 1231 (P=O), 1109 (O-C), 912 (P-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.54–8.13 (m, 26H), 4.67–4.81 (m, 4H), 2.10–2.19 (m, 2-H_{Ar}, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.8 (d, J_{PC} = 124.78 Hz, C-4), 129.5 (C-4a), 128.7 (C-5), 123.9 (C-6), 128.1 (C-7), 122.4 (C-8), 153.9 (C-8a), 132.9 (C-1', C-4'), 116.2 (C-2', C-3', C-5', C-6'), 158.3 (1-C_{Ar}), 118.5 (2-C_{Ar}), 129.6 (3-C_{Ar}), 131.9 (4-C_{Ar}), 124.9 (5-C_{Ar}), 129.4 (6-C_{Ar}), 15.9 (2C, 2CH_3). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 3.49. Anal. calcd. for $C_{34}H_{30}N_2O_6P_2$: C, 65.39; H, 4.84; N, 4.49. Found: C, 65.47; H, 4.92; N, 4.57.

3-[4-[2-(3-Methylphenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphos-phinin-3-yl]phenyl]-2-(2-methylphenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5g). Route (a): Pale brown crystals (2.05 g, 64%); mp 150–152 °C. IR (KBr): $\tilde{\nu}$ 1204 (P=O), 1121 (O-C), 921 (P-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.39–7.97 (m, 26H), 4.72–4.99 (m, 4H), 1.99 (m, 3-H_{Ar}, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.9 (d, J_{PC} =127.55 Hz, C-4), 129.6 (C-4a), 128.6 (C-5), 124.4 (C-6), 128.1 (C-7), 123.1 (C-8), 151.4 (C-8a), 132.4 (C-1', C-4'), 116.7 (C-2', C-3', C-5', C-6'), 155.3 (1-C_{Ar}), 116.3 (2-C_{Ar}), 136.5 (3-C_{Ar}), 132.7 (4-C_{Ar}), 128.9 (5-C_{Ar}), 126.6 (6-C_{Ar}), 20.1 (2C, 2CH_3). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 3.62. Anal. calcd. for $C_{34}H_{30}N_2O_6P_2$: C, 65.39; H, 4.84; N, 4.49. Found: C, 65.51; H, 4.98; N, 4.61.

3-[4-[2-(4-Chloro-3-methylphenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphos-phinin-3-yl]phenyl]-2-(4-chloro-3-methylphenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxaza-phosphine-2-oxide (5h). Route (a): Pale brown crystals (2.22 g, 62%); mp 126–128 °C. IR (KBr): $\tilde{\nu}$ 1210 (P=O), 1119 (O-C), 908 (P-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.51–7.64 (m, 24H), 4.50–4.71 (m, 4H), 1.93 (m, 6H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.9 (d, J_{PC} = 128.41 Hz, C-4), 129.3 (C-4a), 128.4 (C-5), 123.9 (C-6), 128.1 (C-7), 122.4 (C-8), 152.7 (C-8a), 132.6 (C-1', C-4'), 116.7 (C-2', C-3', C-5', C-6'), 154.3 (1-C_{Ar}), 117.9 (2-C_{Ar}), 128.9 (3-C_{Ar}), (4-C_{Ar}), 126.8 (5-C_{Ar}), 128.1 (6-C_{Ar}), 13.4 (2C, 2CH_3). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 4.62. Anal. calcd. for $C_{34}H_{28}Cl_2N_2O_6P_2$: C, 58.89; H, 4.07; N, 4.04. Found: C, 58.97; H, 4.15; N, 4.13.

3-[4-[2-(2,4-Dichlorophenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl]phenyl]-2-(2,4-dichlorophenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5i). Route (a): Colorless crystals (2.53 g, 66%); mp 166–169 °C. IR (KBr): $\tilde{\nu}$ 1224 (P=O), 1113 (O-C), 923 (P-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.34–8.21 (m, 18H), 4.73–5.01 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 46.1 (d, J_{PC} = 127.33 Hz, C-4), 129.6 (C-4a), 128.5 (C-5), 124.1 (C-6), 127.7 (C-7), 123.44 (C-8), 152.1 (C-8a), 132.5 (C-1', C-4'), 117.5 (C-2', C-3', C-5', C-6'), 155.4 (1-C_{Ar}), 116.3 (2-C_{Ar}), 138.3 (3-C_{Ar}), 137.1 (4-C_{Ar}), 128.5 (5-C_{Ar}), 132.1 (6-C_{Ar}). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 1.59. Anal. calcd. for $C_{32}H_{22}Cl_4N_2O_6P_2$: C, 52.34; H, 3.02; N, 3.82. Found: C, 52.39; H, 3.11; N, 3.93.

3-[4-[2-(2,6-Dimethylphenoxy)-2-oxo-3,4-dihydro-2λ^5-benzo[*e*][1,3,2]oxazaphosphinin-3-yl]phenyl]-2-(2,6-dimethylphenoxy)-3,4-dihydrobenzo[*e*][1,3,2]oxazaphosphine-2-oxide (5j). Brown crystals (2.16 g, 64%); mp 140–142 °C. IR (KBr): $\tilde{\nu}$ 1222 (P=O), 1127 (O-C), 917 (P-O) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.41–7.71 (m, 30H), 4.41–4.61 (m, 4H), 1.93–1.99 (m, 2,6-H_{Ar}, 12H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 45.6 (d, J_{PC} = 128.41 Hz, C-4), 129.4 (C-4a), 128.6 (C-5), 124.1 (C-6), 128.0 (C-7), 123.1 (C-8), 152.8 (C-8a), 132.3 (C-1', C-4'), 116.8 (C-2', C-3', C-5', C-6'), 154.3 (1-C_{Ar}), 124.3 (2-C_{Ar}), 126.4 (3-C_{Ar}), 132.4 (4-C_{Ar}), 126.4 (5-C_{Ar}), 138.7 (6-C_{Ar}), 16.3 (4C, 4CH_3). ^{31}P NMR (161.98 MHz, DMSO-d_6): δ 4.62. Anal. calcd. for $C_{36}H_{34}N_2O_6P_2$: C, 66.25; H, 5.25; N, 4.29. Found: C, 66.39; H, 5.33; N, 4.38.

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