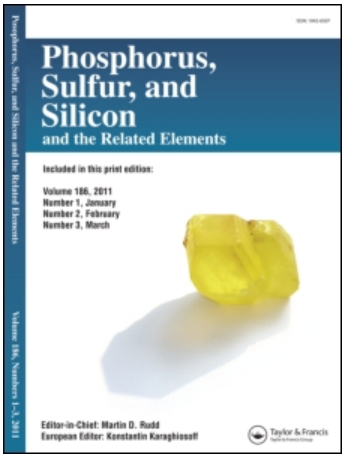

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SYNTHESIS, SPECTRAL, X-RAY DIFFRACTION ANALYSIS AND ANTIMICROBIAL ACTIVITY OF 6-ARYLOXY/TRICHLOROMETHYL/CHLOROETHOXY-12-OXO-DIBENZO[d,g] [1,3,2] DIOXAPHOSPHOCIN 6-OXIDES

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SYNTHESIS, SPECTRAL, X-RAY DIFFRACTION ANALYSIS AND ANTIMICROBIAL ACTIVITY OF 6-ARYLOXY/ TRICHLOROMETHYL/ CHLOROETHOXY-12-OXO-DIBENZO [d,g] [1,3,2] DIOXAPHOSPHOCIN 6-OXIDES

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Syntheses of several 6-aryloxy-12-oxo-dibenzo[d,g][1,3,2] dioxaphosphocin 6-oxides (**3a-i**), trichloromethyl-12-oxo-dibenzo[d,g][1,3,2]dioxaphosphocin 6-oxide (**3j**) and 2-chloroethoxy-12-oxo-dibenzo[d,g][1,3,2]dioxaphosphocin 6-oxide (**3k**) were accomplished by the reaction of equimolar quantities of 2,2′-dihydroxy benzophenone (**1**) with various aryl / alkyl phosphorodichloridates (**2a-i,2k**) and trichloromethyl phosphonicdichloride (**2j**) in the presence of triethylamine at 45–50°C. An X-ray diffraction analysis of 6-(4′-methyl phenoxy)-12-oxo-dibenzo[d,g][1,3,2]dioxaphosphocin 6-oxide(**3d**) revealed that the dioxaphosphocin ring is in distorted-boat conformation with the "oxo" group in a pseudo equatorial arrangement and phosphoryl oxygen (P=O) in equatorial orientation in the solid state. The proposed structures of the title compounds are supported by IR, ^{1}H, ^{13}C and ^{31}P NMR and Mass spectral data. Compounds **3f, 3g, 3h, 3i, 3j** and **3k** are found to possess significant antibacterial and antifungal activity.

Keywords: 6-substituted-12-oxo-dibenzo[d,g][1,3,2] dioxaphosphocin 6-oxides; NMR, mass spectral, x-ray diffraction analysis; antimicrobial activity; distorted-boat conformation

INTRODUCTION

Organophosphorus compounds are ubiquitous in nature and they have unique multifaceted applications[1,2]. Mainly the chemistry of dibenzodioxaphosphocins has gained considerable importance recently because of

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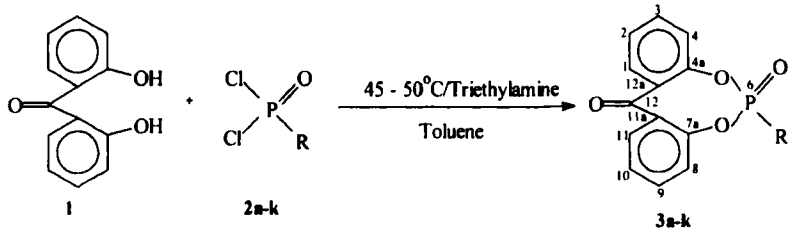
their use as insecticides[1], anti-cancer agents[3] and lubricating oil additives and polymer stabilizers[4]. As part of our continuing investigations[5], we have synthesized a new class of dibenzodioxaphosphocin 6-oxides with an "oxo" group in the ring system. The NMR study and x-ray diffraction analysis indicated various conformations for the dibenzodioxaphosphocin hetero ring depending on the substituents. It is reported that it assumes a boat-chair form in dibenzodioxaphosphocin 6-oxides[6] and dibenzodioxathiophosphocin 6-sulfide[7]. A "distorted-boat-chair" form existed in 2,10-dichloro 6-(2′,3′-dimethyl phenoxy) dibenzo [d,g][1,3,6,2]dioxathiaphosphocin 6-sulfide[8] and a "distorted-boat" conformation was present in the structures of dinaphthodioxathiaphosphocin 8-oxides[9a] and dinaphthodioxaphosphocin 8-oxides[5c&9b]. The members of **3a-k** were characterized by elemental, IR, NMR (^{1}H, ^{13}C and ^{31}P) and mass spectral analysis and tested for their antimicrobial activity.

RESULTS AND DISCUSSION

Syntheses of 6-aryloxy/trichloromethyl and 2-chloroethoxy-12-oxodibenzo [d,g] [1,3,2] dioxaphosphocin 6-oxides (**3 a-i, 3j** and **3k**) was accomplished by the cyclo condensation of equimolar quantities of 2,2′-dihydroxybenzophenone (**1**) with various arylphosphorodichloridates (**2a-i**), trichloromethyl phosphonic dichloride (**2j**) and O-2-chloroethylphosphorylchloride (**2k**) respectively (Scheme 1). Two equivalents of triethylamine as the base in dry toluene as solvent and with temperature ranging between 45–50°C was found to be ideal to effect this cyclo condensations. Purification of these products (**3a-k**) was achieved by filtering the reaction mixture to separate the triethylamine hydrochloride, evaporation of the filtrate in a rotaryevaporator under vacuum to obtain a residue, washing it with water and recrystallization from 2-propanol. Certain physical data along with IR absorptions and elemental analysis are found in Table I. Tables II-V contain ^{1}H, ^{13}C and ^{31}P NMR and mass spectral data for compounds **3a-k**. X-ray diffraction data for the crystal structure **3d** is given in Tables VII -X.

The >C=O showed bands in a relatively low region at 1637–1653 cm^{-1} due to the effect of two aromatic phenyl rings bonded to it. The P=O exhibited bands at 1293–1319 cm^{-1} and the absorptions at 1189–1238 cm^{-1} and 957–985 cm^{-1} were ascribed to (POC-Ar)[10].

The proton NMR spectra (Table II) of members of **3**, exhibited signals for the protons of the two aromatic rings which are attached to C=O group in the range of δ 7.15 -8.10 as complex multiplets [5a,5c&11]. The aryloxy moiety protons of **3 a-i** also exhibited multiplets in the range of δ 6.92–7.43 (Table II) while the protons of the chloroethoxy group (**3k**) appeared as two distinct triplets in the regions δ 4.09–4.20 and δ 3.67 – 3.75.



SCHEME 1

Compd.	*R*	*Compd.*	*R*
3a	C_6H_5O	**3f**	2′-Cl-C_6H_4O
b	2′-H_3C-C_6H_4O	**g**	4′-Cl-C_6H_4O
c	3′-H_3C-C_6H_4O	**h**	2′,4′-Cl_2-C_6H_3O
d	4′-H_3C-C_6H_4O	**i**	2′,6′-Cl_2-C_6H_3O
e	2′,5′-$(H_3C)_2$-C_6H_3O	**j**	Cl_3C
		k	$ClCH_2CH_2O$

The ^{13}C NMR chemical shifts are presented for compounds (**3a-j**) in the Tables III&IV. Oxygen bearing carbons C (4a) and C (7a) gave signals in the range of 147.8 – 149.48 ppm and some of them showed doublets ($^2J_{POC}$ = 6.8 –9.2 Hz)[12]. The doublet in the region 123.52–123.71 ppm ($^3J_{POCC}$ = 3.4 –4.5 Hz) was assigned to C (4) and C(8). Bridged carbons C (11a) and C (12a) exhibited low intensity signals in the range of 126.27–127.08 ppm ($^3J_{POCC}$ = 2.7 –3.2 Hz)[13]. Signals near 134 ppm were assigned to C(3) and C(9) and those at 130 ppm have been ascribed for C(1) and C(11). Low intensity singlets are observed for the carbons C (2) and C (10) at upfield region, 126.72–127.56 ppm. Identification of the bridged carbon (C (12) of the C=O group) is done by observing a signal in the region 187.62–189.99 ppm[14]. The relatively narrow range of the carbon signals for C (4a/7a), C(11a/12a) and C(12) implies that they have similar arrangements in the structures.

TABLE I Physical Properties and IR Spectral Data of Compounds **3a-k**

MF	MP[a]	Yield	Elemental Analysis – Found (Calcd %)		IR (cm^{-1})		
					P=O	P-O-C (aromatic)	
	(°C)	(%)	C	H		P-O	O-C
$C_{19}H_{13}O_5P$	130–132	74	64.63 (64.78)	3.62 (3.72)	1302	965	1195
$C_{20}H_{15}O_5P$	148–150	73	65.74 (65.58)	4.27 (4.13)	1308	985	1235
$C_{20}H_{15}O_5P$	138–140	68	65.47 (65.58)	4.25 (4.13)	1299	969	1221
$C_{20}H_{15}O_5P$	168–170	75	65.36 (65.58)	4.23 (4.13)	1299	968	1189
$C_{21}H_{17}O_5P$	127–130	70	66.52 (66.32)	4.40 (4.51)	1298	957	1206
$C_{19}H_{12}O_5PCl$	170–172	65	58.78 (59.01)	3.02 (3.13)	1315	966	1238
$C_{19}H_{12}O_5PCl$	142–144	68	59.27 (59.01)	3.21 (3.13)	1295	965	1216
$C_{19}H_{11}O_5PCl_2$	158–160	63	54.44 (54.19)	2.78 (2.63)	1298	961	1198
$C_{19}H_{11}O_5PCl_2$	186–88	66	53.96 (54.19)	2.5 (2.63)	1319	952	1199
$C_{14}H_8O_4PCl_3$	148–150	65	44.38 (44.54)	2.02 (2.14)	1308	978	1202
$C_{15}H_{12}O_5PCl$	198–200	50	52.98 (53.20)	3.28 (3.37)	1293	965	1216

-propanol

TABLE II H-1 and P-31 NMR Chemical Shifts for Compounds **3a-k** (δ from TMS and 85% H_3PO_4)

Compd	*Ar-H*	*OAr-H*	*OAr-CH_3*	*^{31}P(NMR)*
3a	7.15–8.06 (m,8H)	7.09–7.16 (m,5H)	–	–13.96
3b	7.18–8.01 (m,8H)	7.04–7.13 (m,4H)	1.98 (s, 3H, 2′-CH_3)	–13.93
3c	7.22–8.07 (m,8H)	7.02–7.11 (m, 4H)	2.16 (s,3H,3′-CH_3)	–13.95
3d	7.24–8.08 (m,8H)	7.11–7.19 (m,4H)	2.18 (s,3H,4′-CH_3)	–13.73
3e	7.26–8.10 (m,8H)	6.92–7.24 (m,3H)	2.0 (s,3H,2′-CH_3) 2.14 (s,3H,5′-CH_3)	–13.97
3f	7.33–8.10 (m,8H)	7.15–7.31 (m,4H)	–	–14.31
3g	7.19–8.09 (m,8H)	6.72–7.10 (m,4H)	–	–
3h	7.42–8.09 (m,8H)	7.26–7.45 (m,3H)	–	–14.38
3i	7.40–8.10 (m,8H)	7.14–7.43 (m,3H)	–	–14.30
3j	7.27–7.92 (m,8H)	–	–	ND
3k	7.21–8.02 (m,8H)	–	4.09–4.20 (t, OCH_2) 3.67–3.75 (t, CH_2Cl)	–4.88

ND = Not determined

The ^{13}C NMR chemical shifts for the 6-aryloxy/trichloromethyl and 2-chloroethoxy groups are illustrated in Table IV, and the ^{31}P chemical shifts are presented in Table II. The low intensity doublet in the range of 146.20–148.40 ppm ($^2J_{POC(1')}$= 8.0–9.2 Hz)was assigned to C (1′)[15]. Both C (2′) and C (6′) displayed doublets ($^3J_{POCC(2',6')}$=2.3–5.7 Hz) with varying intensities depending upon substitutions. An upfield shift of approximately 5 ppm was noted for the C(2′) methyl carbon in **3b** possibly due to a γ-interaction with non-bonded electrons of the exocyclic oxygen atom[5a,12].

TABLE III C-13 NMR Chemical Shifts for Compounds **3a – J** (ppm values from TMS)[a]

C-1 & C-11	*Carbon atoms*		*C-4 & C-8*	*C-4a & C-7a*	*C-11a & C-12a*
	C-2 & C-10	*C-3 & C-9*			
130.37	127.26	134.83	123.71 (3.4)	150.33 (6.8)	126.27
131.63	126.87	134.39	123.51 (3.5)	149.48	126.87
129.68	126.72	134.47 (2.3)	123.52 (3.5)	149.75	126.89
130.42	126.88	134.44	123.50 (4.5)	–	126.88
131.30	126.87	134.43	123.61 (3.5)	148.75	126.85 (2.7)
130.95	126.72	134.52	123.61 (3.5)	147.92 (9.2)	127.02
129.49	126.85	134.21	123.64	147.42	126.74
130.69	127.16	134.58	123.54	147.80 (9.1)	128.22
129.27	127.02	134.53	123.66 (3.4)	148.32	127.08 (3.2)
132.12	127.56	134.45	123.20	147.98	126.45

constants (J_{PC}) are in Parentheses in Hz.

TABLE IV C-13 NMR Chemical Shifts for Compounds **3a-J** with aryl moiety (ppm values from TMS)[a]

Compd	*C-1′*	*C-2′*	*C-3′*	*C-4′*	*C-5′*	*C-6′*	*-CH₃*
3a	148.4 (9.0)	120.02 (4.5)	132.98	123.81	132.98	120.02 (4.5)	–
3b	148.10 (9.2)	129.04	131.78	125.84	127.27	119.31 (2.3)	15.98 (C-2′)
3c	147.89	120.24 (5.7)	139.50	126.72	132.65	116.60 (5.7)	21.32 (C-3′)
3d	148.17	119.36 (5.6)	132.62	135.64	132.62	119.36 (5.6)	20.73 (C-4′)
3e	148.20 (8.0)	125.62	131.86	126.59	137.47	119.92	15.57 & 20.93 (C-2′ & C-5′)
3f	146.20	131.70	128.09	128.09	132.63	120.93 (2.3)	–
3g	146.43	128.05	127.9	131.56	129.54	116.62	–
3h	147.45	125.39	131.72 (3.5)	132.73	132.73	121.83	–
3i	147.64	132.56 (2.3)	–	–	132.57	132.56 (2.3)	–
3j	–	–	–	–	–	–	100.05

a. Coupling constants (J_{pc}) are in parentheses in Hz.

The ^{31}P NMR signals appeared within the region from −14.38 to −13.73 ppm for **3a-i** and −4.88 ppm for **3k** from 85% phosphoric acid[5a]. Mass spectral analyses were conducted for a few compounds (Table V) and the data were confirmatory for the molecular ions of compounds **3c-f, 3h** and **3j**. Important common ions observed in **3** are $[M^{+\cdot} - CO]^{+}$, $[M^{+\cdot} - OR]^{+}$, $[(M^{+\cdot} - {}^{\cdot}OR) - CHO]^{+}$ and $[(M^{+\cdot} - {}^{\cdot}OR) - PO_2]^{+}$.

The structure of crystalline (**3d**) was determined by x-ray diffraction analysis in an attempt to establish the geometrical features of the system with "oxo" group at central carbon of the heterocyclic ring and to confirm its identity. White transparent needle shaped single crystals were obtained by slow evaporation of a solution of **3d** in 2-propanol. A view of the molecule (Figure 1) drawn by ORTEP[16]shows atomic designation and relative configuration of the assymmetric unit.

TABLE V Mass Spectral [EI] m/z Values (% Important Ions) for **3c -f, 3h** and **3j**

Compd	*m/z Values*
3c	366 366[100; $M^{+\cdot}$], 338 [11; (M^+ – CO)], 259 [2.5; (M^+- C_7H_7O)], 230 [14; (M^+- C_7H_7O) – CHO], 196 [49; (M^+ – $C_7H_7O_3P$)], 168 [17.5; (M^+ – $C_7H_7O_3P$) – CO], 139 [16; (M^+- C_7H_7OP) – CHO], 92 [17.5].
3d	366 366[91; $M^{+\cdot}$], 338 [5; (M^+-CO)], 259 [5; (M^+-C_7H_7O)], 230 [13; (M^+-C_7H_7O)- CHO], 196 [51; (M^+- $C_7H_7O_3P$)], 168 [23; (M^+- $C_7H_7O_3P$) – CO], 139 [23.4; (M^+-$C_7H_7O_3P$) – CHO], 107[100; (M^+- $C_{13}H_8O_4P$)], 92 [23.4], 77[35].
3e	380 380[100; $M^{+\cdot}$], 365 [42; (M^+- CH_3)], 351 [29; (M^+- C_2H_5)], 337 [14; (M^+- CH_3)- CO], 286 [71], 2/6 [36; (M^+- C_8H_8)], 259 [52; (M^+ – C_8H_9O)], 248 [10; (M^+- C_8H_8)-CO], 196 [56; (M^+- $C_8H_9O_3P$)], 168 [20; (M^+- $C_8H_9O_3P$) – CO], 139 [26], 122 [31], 104 [57], 77 [45].
3f	386 386[29; $M^{+\cdot}$], 351 [100; (M^+- Cl)], 323 [20; (M^+- Cl)-CO], 275 [2.5; (M^+ – C_6H_4Cl)], 259 [2.5; (M^+- C_6H_4OPCl)], 215 [19], 196 [32.5; (M^+- $C_6H_4O_3PCl$)], 168 [31.6; (M^+-$C_6H_4O_3PCl$) – CO], 139 [52.5], 92 [54].
3h	420 420[71, 46, 4; $M^{+\cdot}$, $(M^{+\cdot}+2)$, $(M^{+\cdot}+4)$], 385 [100, 42.5; (M^+-Cl), (M^++2)-Cl], 357 [17; (M^+- Cl) – CO], 276 [8.8; (M^+- $C_6H_2Cl_2$)], 259 [15; M^+- $C_6H_3Cl_2O$], 215 [21], 196 [51; (M^+- $C_6H_3OPCl_2$)], 168 [33; (M^+ – $C_6H_3OPCl_2$) – CO], 139 [37.5], 114 [46], 92 [32.5].
3J	376 376[10.3; $M^{+\cdot}$, $(M^{+\cdot}+2)$], 233 [7.5], 222 [12.5], 197 [100; (M^+-OP(O) CCl_3)], 169 [25; (M^+-OP(O)CCl_3)-CO], 140 [11], 120 [10].

TABLE VI Antimicrobial Activity of 6-Substituted –12-oxo-dibenzo [d,g] [1,3,2] dioxaphosphocin 6-oxides **3a-k**

Compd	*Zone of Inhibition (mm)*					
	Fungi				*Bacteria*	
	Curvularia lunata		*Aspergillus niger*		*Bacillus subtilis*	*Klebsiella pneumoniae*
	500[a]	*1000*[a]	*500*[a]	*1000*[a]	*1000*[a]	*1000*[a]
3a	-[b]	–	–	–	–	–
3b	–	–	–	–	–	–
3c	–	–	–	–	–	–
3d	–	–	–	–	–	–
3e	–	–	–	–	–	–
3f	12	22	15	24	22	24
3g	10	18	13	20	20	22

Compd	Zone of Inhibition (mm)					
	Fungi				Bacteria	
	Curvularia lunata		*Aspergillus niger*		*Bacillus subtilis*	*Klebsiella pneumoniae*
	500[a]	1000[a]	500[a]	1000[a]	1000[a]	1000[a]
3h	11	20	9	17	11	19
3i	13	24	11	18	14	22
3j	12	18	14	20	15	17
3k	10	16	10	18	22	24

a. Concentration in ppm.
b. The "-" indicates no activity at the concentrations specified.

TABLE VII(A) Final Positions and Thermal Parameters: Atomic coordinates (x 10^{-4}) and equivalent isotropic displacement parameters ($A^{o2} \times 10^{-3}$) for non-H atoms[(A)]

Atom	x	y	z	U(eq)
O(1)	4199(1)	8340(1)	534(3)	45(1)
P(2)	4818(1)	8626(1)	1296(1)	41(1)
O(3)	4786(1)	9424(1)	950(2)	40(1)
C(4)	4394(1)	9852(2)	1851(4)	40(1)
C(5)	3750(1)	9883(2)	1610(4)	44(1)
C(6)	3372(1)	9526(2)	360(4)	49(1)
C(7)	3647(1)	9169(2)	−1055(4)	42(1)
C(8)	4027(1)	8594(2)	−981(4)	40(1)
C(9)	4692(2)	10250(2)	2985(4)	52(1)
C(10)	4350(2)	10690(2)	3912(5)	68(1)
C(11)	3714(2)	10727(2)	3737(5)	74(1)
C(12)	3418(2)	10334(2)	2599(5)	62(1)
O(13)	2806(1)	9559(2)	424 (3)	81(1)
C(14)	3463(2)	9390(2)	−2567(4)	55(1)
C(15)	3666(2)	9049(2)	−3902(5)	63(1)
C(16)	4046(2)	8482(2)	−3773(5)	61(1)
C(17)	4225(2)	8242(2)	−2306(4)	52(1)
O(18)	5336(1)	8395(1)	105(3)	53(1)

Atom	*x*	*y*	*z*	*U(eq)*
C(19)	5965(1)	8276(2)	533(4)	46(1)
C(20)	6230(2)	7688(2)	−68(6)	70(1)
C(21)	6853(2)	7559(2)	350(6)	81(1)
C(22)	7194(2)	7998(2)	1300(5)	64(1)
C(23)	6913(2)	8594(2)	1777(5)	65(1)
C(24)	6297(2)	8735(2)	1403(5)	60(1)
C(25)	7858(2)	7823(4)	1750(10)	98(2)
O(26)	4886(1)	8419(1)	2929(3)	55(1)

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor. [(A)] Estimated standard deviations are given in parentheses.

TABLE VII(B) Final Positions and Thermal Parameters: Anisotropic displacement parameters ($A^{o2} \times 10^{-3}$) for non-H atoms[a]. The anisotropic displacement factor exponent takes the form: -2 pi^2 [H^2 a*^2 U11 + ... + 2 H k a* b* U12]

Atom	*U11*	*U22*	*U33*	*U23*	*U13*	*U12*
O(1)	49(1)	40(1)	48(1)	8(1)	0(1)	−5(1)
P(2)	44(1)	40(1)	39(1)	2(1)	1(1)	2(1)
O(3)	38(1)	40(1)	43(1)	2(1)	4(1)	−2(1)
C(4)	47(2)	35(2)	39(2)	−1(1)	7(1)	−3(1)
C(5)	45(2)	43(2)	44(2)	−2(1)	6(1)	1(1)
C(6)	40(2)	56(2)	51(2)	1(2)	−1(2)	5(2)
C(7)	36(2)	45(2)	45(2)	−3(2)	−4(1)	−6(1)
C(8)	38(2)	40(2)	43(2)	1(1)	−1(1)	−10(1)
C(9)	49(2)	49(2)	56(2)	−5(2)	1(2)	−5(2)
C(10)	84(3)	59(2)	61(3)	−18(2)	3(2)	−4(2)
C(11)	84(3)	67(3)	71(3)	−24(2)	13(2)	13(2)
C(12)	54(2)	65(2)	68(2)	−10(2)	5(2)	13(2)
O(13)	37(1)	118(2)	86(2)	−26(2)	−2(1)	6(1)
C(14)	55(2)	53(2)	56(2)	3(2)	−11(2)	−6(2)
C(15)	77(3)	70(3)	41(2)	4(2)	−10(2)	−16(2)
C(16)	68(2)	71(3)	45(2)	−14(2)	1(2)	−16(2)
C(17)	54(2)	49(2)	54(2)	−13(2)	4(2)	−10(2)

Atom	*U11*	*U22*	*U33*	*U23*	*U13*	*U12*
O(18)	47(1)	64(2)	47(1)	−8(1)	−2(1)	14(1)
C(19)	46(2)	43(2)	49(2)	−2(2)	3(2)	7(2)
C(20)	61(2)	65(3)	85(3)	−14(2)	11(2)	12(2)
C(21)	63(2)	67(3)	113(4)	−19(3)	11(3)	23(2)
C(22)	47(2)	69(2)	77(3)	13(2)	3(2)	7(2)
C(23)	53(2)	63(2)	80(3)	−3(2)	−10(2)	−1(2)
C(24)	59(2)	44(2)	77(3)	−12(2)	−2(2)	10(2)
C(25)	50(2)	127(5)	118(5)	23(4)	4(3)	16(3)
O(26)	70(2)	54(1)	42(1)	6(1)	−1(1)	0(1)

a. Estimated standard deviations are given in parentheses.

TABLE VIII Bond Lengths for Non-Hydrogen[a] (in Å)

Bond	*Distance*	*Bond*	*Distances*
P(2)-O(26)	1.440(2)	C(6)-C(5)	1.496(5)
P(2)-O(18)	1.559(2)	C(5)-C(4)	1.392(4)
P(2)-O(1)	1.573(2)	C(5)-C(12)	1.401(5)
P(2)-O(3)	1.575(2)	C(12)-C(11)	1.378(6)
O(13)-C(6)	1.213(4)	C(11)-C(10)	1.368(6)
O(1)-C(8)	1.416(4)	C(10)-C(9)	1.369(5)
O(3)-C(4)	1.404(4)	C(9)-C(4)	1.382(5)
O(18)-C(19)	1.411(4)	C(19)-C(24)	1.354(5)
C(8)-C(17)	1.374(5)	C(19)-C(20)	1.370(5)
C(8)-C(7)	1.381(4)	C(24)-C(23)	1.382(5)
C(17)-C(16)	1.375(5)	C(23)-C(22)	1.363(5)
C(16)-C(15)	1.370(6)	C(22)-C(21)	1.376(6)
C(15)-C(14)	1.375(5)	C(22)-C(25)	1.509(6)
C(14)-C(7)	1.400(5)	C(21)-C(20)	1.401(6)
C(7)-C(6)	1.498(4)		

a. Estimated standard deviations are given in parentheses.

TABLE IX Bond Angles for Non-Hydrogen[a] (in°)[a]

Bond	*Angle*	*Bond*	*Angle*
O(26)-P(2)-O(18)	117.57(13)	C(5)-C(6)-C(7)	124.1(3)
O(26)-P(2)-O(1)	112.09(14)	C(4)-C(5)-C(12)	116.1(3)
O(18)-P(2)-O(1)	103.56(13)	C(4)-C(5)-C(6)	128.0(3)
O(26)-P(2)-O(3)	117.05(14)	C(12)-C(5)-C(6)	115.7(3)
O(18)-P(2)-O(3)	101.14(13)	C(11)-C(12)-C(5)	121.7(4)
O(1)-P(2)-O(3)	103.54(12)	C(10)-C(11)-C(12)	120.1(4)
C(8)-O(1)-P(2)	117.6(2)	C(11)-C(10)-C(9)	120.1(4)
C(4)-O(3)-P(2)	120.5(2)	C(10)-C(9)-C(4)	119.7(4)
C(19)-O(18)-P(2)	124.0(2)	C(9)-C(4)-C(5)	122.2(3)
C(17)-C(8)-C(7)	123.0(3)	C(9)-C(4)-O(3)	115.3(3)
C(17)-C(8)-O(1)	118.6(3)	C(5)-C(4)-O(3)	122.5(3)
C(7)-C(8)-O(1)	118.3(3)	C(24)-C(19)-C(20)	122.0(3)
C(16)-C(17)-C(8)	118.4(4)	C(24)-C(19)-O(18)	122.1(3)
C(15)-C(16)-C(17)	120.5(4)	C(20)-C(19)-O(18)	115.8(3)
C(16)-C(15)-C(14)	120.5(4)	C(19)-C(24)-C(23)	119.6(3)
C(15)-C(14)-C(7)	120.5(4)	C(22)-C(23)-C(24)	121.3(4)
C(8)-C(7)-C(14)	117.0(3)	C(23)-C(22)-C(21)	117.6(4)
C(8)-C(7)-C(6)	124.6(3)	C(23)-C(22)-C(25)	122.1(5)
C(14)-C(7)-C(6)	118.1(3)	C(21)-C(22)-C(25)	120.4(5)
O(13)-C(6)-C(5)	118.9(3)	C(22)-C(21)-C(20)	122.7(4)
O(13)-C(6)-C(7)	116.8(3)	C(19)-C(20)-C(21)	116.7(4)

a. Estimated standard deviations are given in parentheses.

The final positional (fractional) parameters for non-hydrogen atoms of **3d**, bond lengths and bond angles excluding hydrogens are listed in Tables VII, VIII and IX respectively. In the dioxaphosphocin ring system the bond lengths of the two P-O-C-C-C=O fragments are equal within the limits of error, but not their bond angles. The "endo" cyclic P-O bond distances are longer than "exo" cyclic P-O bond lengths and the P=O bond lengths are comparable to the corresponding values observed in the similar

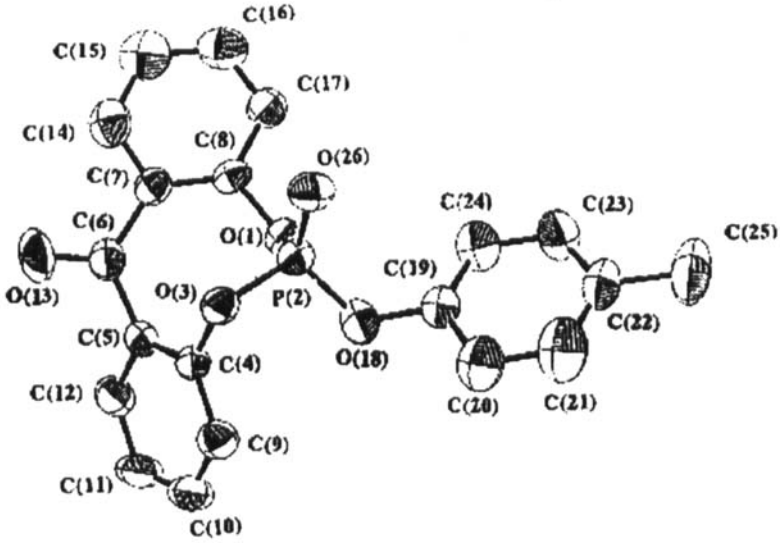


FIGURE 1 A perspective view of the molecule along with the numbering scheme, Showing distorted boat (DB) conformation. Ellipsoids are plotted at the 50% probability level

type of structures[6,9]. But these values are significantly less than those which are observed for the structures of dibenzo substituted dioxathiaphosphocin 6-sulfides[8]. An important and interesting feature is that the corresponding endo cyclic bond angles between the two P-O-C-C-C=O fragments of the ring significantly differ from each other, whereas the same angles are found equal to each other in the respective fragments in the structures of similar 8-membered rings[5c]. This indicates, that the heterocyclic ring experiences strain due to the presence of highly electronegative "Oxygen" in the C=O.

In the structure **3d** the dioxaphosphocin ring assumes a distorted-boat conformation which is evident from its ring torson angles given in Table X and also from the deviations of the atoms P (2)=-0.250, O (1) = –0.681, C (5)= –0.368 and C (6) = –0.316 on one side and O (3) = 0.675, C (4) = 0.115, C (7) = 0.508 and C (8) = 0.316 on the other side of the mean plane passing through the ring atoms. However, it is observed that this form is differing from the generally found "boat-chair" or distorted-boat-chair' form for the heterocyclic ring of the structures [6,7 & 8]. Thus the oxygen of the carbonyl (C=O) group of the heterocyclic ring is

defining the conformation of the 8-membered ring in dibenzodioxaphosphocin 6-oxide in **3d**.

TABLE X Selected Torsion Angles (in deg.) (e.s. d's in paranthesis)

Atoms	*Angle*
O(26) -P(2) -O(1) -C(8)	170.3(2)
O(18) -P(2) -O(1) -C(8)	-62.0(2)
O(3) -P(2) -O(1) -C(8)	43.2(2)
O(26) -P(2) -O(3) -C(4)	-47.2(3)
O(18) -P(2) -O(3) -C(4)	-176.3(2)
O(1) -P(2) -O(3) -C(4)	76.6(2)
O(26) -P(2) -O(18) -C(19)	-28.8(3)
O(1) -P(2) -O(18) -C(19)	-153.0(2)
O(3) -P(2) -O(18) -C(19)	100.0(3)
P(2) -O(1) -C(8) -C(17)	91.9(3)
P(2) -O(1) -C(8) -C(7)	-90.7(3)
C(7) -C(8) -C(17) -C(16)	1.3(5)
O(1) -C(8) -C(17) -C(16)	178.6(3)
C(8) -C(17) -C(16) -C(15)	-1.6(5)
C(17) -C(16) -C(15) -C(14)	0.5(6)
C(16) -C(15) -C(14) -C(7)	0.9(6)
C(17) -C(8) -C(7) -C(14)	0.1(5)
O(1) -C(8) -C(7) -C(14)	-177.2(3)
C(17) -C(8) -C(7) -C(6)	173.9(3)
O(1) -C(8) -C(7) -C(6)	-3.4(4)
C(15) -C(14) -C(7) -C(8)	-1.2(5)
C(15) -C(14) -C(7) -C(6)	-175.4(3)
C(8) -C(7) -C(6) -O(13)	-120.3(4)
C(14) -C(7) -C(6) -O(13)	53.4(4)
C(8) -C(7) -C(6) -C(5)	64.3(4)
C(14) -C(7) -C(6) -C(5)	-121.9(3)

Atoms	*Angle*
O(13) -C(6) -C(5) -C(4)	172.9(3)
C(7) -C(6) -C(5) -C(4)	−11.9(5)
O(13) -C(6) -C(5) -C(12)	−11.3(5)
C(7) -C(6) -C(5) -C(12)	164.0(3)
C(4) -C(5) -C(12) -C(11)	0.3(5)
C(6) -C(5) -C(12) -C(11)	−176.0(4)
C(5) -C(12) -C(11) -C(10)	0.9(7)
C(12) -C(11) -C(10) -C(9)	−1.7(7)
C(11) -C(10) -C(9) -C(4)	1.2(6)
C(10) -C(9) -C(4) -C(5)	0.0(5)
C(10) -C(9) -C(4) -O(3)	179.3(3)
C(12) -C(5) -C(4) -C(9)	−0.8(5)
C(6) -C(5) -C(4) -C(9)	175.1(3)
C(12) -C(5) -C(4) -O(3)	180.0(3)
C(6) -C(5) -C(4) -O(3)	−4.2(5)
P(2) -O(3) -C(4) -C(9)	103.5(3)
P(2) -O(3) -C(4) -C(5)	−77.1(3)
P(2) -O(18) -C(19) -C(24)	−49.0(4)
P(2) -O(18) -C(19) -C(20)	134.8(3)
C(20) -C(19) -C(24) -C(23)	−3.5(6)
O(18) -C(19) -C(24) -C(23)	−179.5(3)
C(19) -C(24) -C(23) -C(22)	−0.7(6)
C(24) -C(23) -C(22) -C(21)	3.8(6)
C(24) -C(23) -C(22) -C(25)	−177.6(5)
C(23) -C(22) -C(21) -C(20)	−3.1(7)
C(25) -C(22) -C(21) -C(20)	178.3(5)
C(24) -C(19) -C(20) -C(21)	4.1(6)
O(18) -C(19) -C(20) -C(21)	−179.7(4)
C(22) -C(21) -C(20) -C(19)	−0.7(7)

TABLE XI Hydrogen coordinates (10^{-4}) and isotropic displacement parameters ($Å^2 \times 10^{-3}$)[a]

Atom	*x*	*y*	*z*	*U(eq)*
H(9)	5164(15)	10220(16)	3087 (36)	49(9)
H(10)	4517(20)	10938(22)	4686(54)	89(15)
H(11)	3455(20)	11022(22)	4464(52)	97(14)
H(12)	2950(18)	10378(18)	2448(39)	61(10)
H(14)	3164(16)	9794(18)	-2621(38)	58(10)
H(15)	3582(17)	9232(19)	-4903(50)	72(11)
H(16)	4181(17)	8232(19)	-4630(49)	70(12)
H(17)	4496(16)	7821(19)	-2203(42)	63(10)
H(20)	6033(49)	7445(61)	983(126)	321(52)
H(21)	7010 (18)	7111(23)	-58(50)	89(13)
H(23)	7163(23)	8944(24)	2407(54)	106(16)
H(24)	6110(16)	9143(19)	1748(42)	62(10)
H(25A)	8114(29)	7741(33)	862(74)	148(24)
H(25B)	7863(24)	7529(30)	2663(70)	121(21)
H(25C)	8088(40)	8159(44)	2229(97)	195(39)

a. Estimated standard deviations are given in parentheses.

ANTIMICROBIAL ACTIVITY

The compounds **3a-k** were screened for antifungal activity on *Aspergillus niger* and *Curvularia lunata* at concentrations of 500 ppm and 1000 ppm[17] (Table VI). Some of the agents exhibited significant toxicity against both fungi. Their antibacterial activity was also assessed on *Bacillus subtilis* and *Klebsiella pneumoniae*[18] (Table VI). Agents **3f**, **3g**, **3h**, **3i**, **3j**, and **3k** displayed strong action against the both fungi and bacteria.

CONCLUSIONS

In Summary, a simple method for the synthesis of dibenzodioxaphosphocin 6-oxides from the readily available starting materials has been developed and a distorted-boat conformation for the 8-membered dibenzo-

dioxaphosphocin ring has been established. Some of these rare phosphorus heterocycles possess significant antifungal and antibacterial activity.

TABLE XII Bond Lengths and Bond Angles for Hydrogen[a]

(A) Bond lengths (in Å)

Bond	*Distance*	*Bond*	*Distances*
C(17)-H(17)	1.01(4)	C(24)-H(24)	0.93(4)
C(16)-H(16)	0.92(4)	C(23)-H(23)	1.01(5)
C(15)-H(15)	0.93(4)	C(21)-H(21)	0.99(4)
C(14)-H(14)	1.01(4)	C(20)-H(20)	1.09(11)
C(12)-H(12)	1.01(4)	C(25)-H(25A)	0.94(6)
C(11)-H(11)	1.00(4)	C(25)-H(25B)	0.96(6)
C(10)-H(10)	0.89(4)	C(25)-H(25C)	0.91(8)
C(9)-H(9)	1.01(3)		

(B) Bond Angles (in°)[a]

Bond	*Angle*	*Bond*	*Angle*
C(16)-C(17)-H(17)	121(2)	C(4)-C(9)-H(9)	119(2)
C(8)-C(17)-H(17)	121(2)	C(19)-C(24)-H(24)	120(2)
C(15)-C(16)-H(16)	123(2)	C(23)-C(24)-H(24)	120(2)
C(17)-C(16)-H(16)	116(2)	C(22)-C(23)-H(23)	119(3)
C(16)-C(15)-H(15)	119(2)	C(24)-C(23)-H(23)	119(3)
C(14)-C(15)-H(15)	120(2)	C(22)-C(21)-H(21)	124(2)
C(15)-C(14)-H(14)	122(2)	C(20)-C(21)-H(21)	113(2)
C(7)-C(14)-H(14)	117(2)	C(19)-C(20)-H(20)	84(6)
C(11)-C(12)-H(12)	120(2)	C(21)-C(20)-H(20)	95(6)
C(5)-C(12)-H(12)	119(2)	C(22)-C(25)-H(25A)	113(4)
C(10)-C(11)-H(11)	121(2)	C(22)-C(25)-H(25B)	110(3)
C(12)-C(11)-H(11)	119(2)	H(25A)-C(25)-H(25B)	122(5)
C(11)-C(10)-H(10)	117(3)	C(22)-C(25)-H(25C)	117(6)
C(9)-C(10)-H(10)	123(3)	H(25A)-C(25)-H(25C)	99(6)
C(10)-C(9)-H(9)	121(2)	H(25B)-C(25)-H(25C)	94(6)

a. Estimated standard deviations are given in parentheses.

TABLE XIII Mean Planes for the Rings

Plane number (1):			
(L=0.4799370	M=0.4808118	N=-0.7338124	D=12.43376)
*P	-.250(2)		
*O3	-.681(2)		
*O4	.675(2)		
*C1	.316(3)		
*C6	.508(3)		
*C7	-.316(3)		
*C8	-.368(3)		
*C13	.115(3)		
r.m.s.deviation of fitted atoms from plane		.4454 (.0028)	
Plane number(2):			
(L=0.8078241	M=0.5879321	N=-0.04190630	D=16.78263)
*C1	.003(3)		
*C2	-.009(4)		
*C3	.007(4)		
*C4	.002(4)		
*C5	-.008(4)		
*C6	.005(3)		
r.m.s.deviation of fitted atoms from plane		.0062 (.0038)	
Plane number (3):			
(L=0.1228811	M=0.7316043	N=-0.6705635	D=14.08860)
*C8	.006(4)		
*C9	.000(4)		
*C10	-.007(4)		
*C11	.009(4)		
*C12	-.002(4)		
*C13	-.005(4)		
r.m.s.deviation of fitted atoms from plane		.0056 (.0038)	

Plane number (4):

(L=0.3015471	M=0.4784170	N=-0.8247342	D=11.17818)
05	-.0241		
*C14	-.026(3)		
*C15	.010(4)		
*C16	.016(4)		
*C17	-.024(4)		
*C18	.008(5)		
*C19	.017(5)		
C20	-.0713		

r.m.s.deviation of fitted atoms from plane .0181 (.0042)

Dihedral angle between least squares planes (in °):

Planes:	1 & 2	1 & 3	1 & 4	2 & 3	2 & 4	3 & 4
Angle:	45.5	25.5	11.5	56.1	55.98	19.9

EXPERIMENTAL

General

All Melting points were determined on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed at the Central Drug Research Institute, Lucknow, India. IR spectra were recorded as KBr pellets on a Perkin-Elmer 1000 unit. The ^{1}H, ^{13}C and ^{31}P NMR spectra were taken on Varian XL-300 spectrometer operating at 300 MHz for ^{1}H, 75.46 MHz for ^{13}C and 121.48 MHz for ^{31}P. All NMR spectra were recorded using $CDCl_3$ with TMS as the internal reference for ^{1}H & ^{13}C and 85% H_3PO_4 as external standard for ^{31}P NMR spectra. Electron Impact Mass Spectra were recorded on a VG 70–70H instrument at 70eV.

Preparation of 6-(4′-Methyl phenoxy)-12-oxo-dibenzo [d,g][1,3,2] dioxaphosphocin 6-oxide (3d)

A solution of 4-methylphenyl phosphorodichloridate (**2d**, 2.25 g, 0.01 mol) in 20 mL of dry toluene was added over a period of 20 minutes

at 0°C to a stirred solution of 2,2′ – dihydroxy benzophenone (**1**, 2.14 g, 0.01 mol) and triethylamine (2.02 g, 0.02 mol) in 50 mL of dry toluene. After completion of the addition the temperature of the reaction mixture was raised to 45–50°C and kept for 5–6 h with stirring. The progress of the reaction mixture was monitored by TLC analysis. The precipitated triethylamine hydrochloride was filtered and the filtrate was evaporated in a rotaevaporator under vacuum. The residue obtained was washed with water followed by chilled 2-propanol. Colourless crystals were obtained by recrystalization of the product from 2-propanol, to yield 2.67 g (75%) of **3d**, m.p. 168–170°C.

Compounds **3a-c** and **3e-k** were synthesized by adopting the above procedure and the synthetic data for **3a-k** is given in the Table I-V.

CRYSTAL STRUCTURE DETERMINATION

A colourless crystal with dimensions point 0.3x0.2x0.25 (mm) of **3d** was used for data collection with preliminary crystal data being determined via the *weissenberg* technique. Accurate cell dimensions were subsequently refined from least squares procedure using 25 reflections measured ($25°<\theta<35°$) with Enraf- Nonius CAD – 4 diffractometer.

Crystal data were: $C_{20}H_{15}O_5P$, M.W = 366, Orthorhombic, Space group Pbca, a=21.380 (1), b=19.388 (1), C=8.420 (2) Å, V=3490.3 (5) $Å^3$, Z=8, D_x = 1.394 g/cm^3, F(000) = 1520, monochromatic (graphite) MoKα (λ = 0.71073 Å), R = 0.0505 and R_w =0.1151, S=1.045.

A total number of 2679 independent reflections were taken by the w/2θ scan technique with $2\theta<50°$ at T= 293 K. After Lorentz and polarization corrections 2677 reflections were found significant with $I>2\sigma$ (I). No obsorption corrections were obtained. The structure was determined by direct methods using the program SHELXS-86[19]and refined by full-matrix least squares method using the program SHELXL-93[20]. The hydrogen atoms of the structure were located from the difference fourier maps and their parameters were refined isotropically. An R-factor of 0.0505 was obtained by applying a unit weighting scheme and R_w was 0.1151.

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