Synthesis of new class of phosphorus and oxygen macroheterocycles

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New class of macrocyclic aryloxy phosphoranes (**10a–d, 11a–d, 12a–d**) were prepared by reactants the bifunctional synthons (**7–9**) with bis(2/3-chloroalkyl)phenyl triester of phosphoric acid (**5a–d**) in the presence of aq.NaOH in *n*-BuOH in moderate yields. Their chemical structures were established by analytical and spectral (IR, ^{1}H, ^{13}C and ^{31}P and Mass) data.

Keywords: macrocyclic aryloxyphosphorane, bis(2/3-chloroalkyl)phenyl triester of phosphoric acid

Phosphorus containing macrocycles are interesting molecules with potential application in supramolecular and synthetic organic chemistry.[1] They have been synthesised as phosphine oxides, phosphines, phosphonium salts, phosphates, phosphonates and phosphoranes.[2] The importance of these molecules, as phosphorus analogues of crown ethers, is derived from their potential catalytic activity and ion carrying properties. The design of host molecules capable of binding neutral organic molecules as guests is an area of rapidly expanding interest,[3] Cram,[4] Lehn,[5] Vogtle,[6] Diederich[7] and others have made significant advances in this field of host-guest complexation.[8] Our past and present research has led to the construction of phosphoran macrocycles with large preorganised macrocyclic cavities bearing concave functionalities.[9] They are expected to function as good 'hosts' in the 'host-guest chemistry'. This particular property enables them to carry certain metal ion species and drug molecules in the living system. In view of these and several other possible applications phosphorus macroheterocycles with oxygens as donor atoms, have been synthesised.

Results and discussion

Reaction of 2- or 4-methylphenyl phosphorodichloridates (**1** or **2**) with 2-chloroethan-1-ol or 3-chloropropan-1-ol in refluxing toluene in the presence of triethylamine (TEA) afforded corresponding bis(2/3-chloroalkyl)phenyl triester of phosphoric acid **5a–d**. Which on reaction with 2,2'-dihydroxybinaphthyl (**7**), bis(2-hydroxy-1-napthyl)methane (**8**), 5,5'-dichloro-2,2'-dihydroxybiphenyl sulfide (**9**) in the presence of NaOH in *n*-butanol at refluxing temperature yielded the title compounds, **10a–d**, **11a–d** and **12a–d** respectively with moderate yield.

All compounds (**10a–d, 11a–d, 12a–d**) exhibited characteristic IR absorptions[10-13] (Table 1) for P=O and P–O–C$_{ar}$ groups. The aromatic protons showed complex multiplets in the region δ 6.92–7.45. The triplets at δ 4.66–4.28 and δ 3.65–3.30 are attributed for (P)–O–CH$_2$ and (Ar)–O–CH$_2$ respectively. The multiplets at δ 2.23–2.37 are attributed for central-CH$_2$[14] (Table 2). The ^{13}C NMR chemical shifts of **10a**, **11d** and **12d** (Tables 3, 4 and 5) assigned by comparison with carbon chemical shifts of **5a–d** appeared in the expected region.[15-17] The title compounds exhibited two ^{31}P NMR signals,[18,19] δ1.01–5.21 and the other 4.12–11.04 (Table 1). This indicates that they exist two isomers in solution.

The GC–MS spectra of **10a**, **12a** and **12d** (Table 6) shows of $M^{+\bullet}$ at the appropriate molecular weights, [$M-C_7H_{14}O_2^{\bullet}$] at *m/z* 396, [$M-C_7H_{17}O_4^{\bullet}$] at *m/z* 361, [$M-C_{11}H_{12}O_4P$] at *m/z* 281, [$M-C_{11}H_{15}O_6P^{\bullet}$] at *m/z* 252, [$M-C_{20}H_{15}O_2^{\bullet}$] at *m/z* 239,

Table 1 Physical, IR and ^{31}P spectral data of phosphorus and oxygen macroheterocycles (**10a–d, 11a–d, 12a–d**)

Compd	Yield/%	M.p./°C	Molecular formula	Calcd(found) (%)		IR (cm^{-1})		^{31}P NMR (δ)
				C	H	P=O	P–O–C	
10a	68	218–219	$C_{31}H_{27}O_6P$	70.61 (70.73)	5.02 (5.15)	1274	1212, 940	2.42, 11.45
10b	71	210–213	$C_{31}H_{27}O_6P$	70.61 (70.69)	5.02 (5.13)	1273	1208, 942	2.31, 11.22
10c	63	187–190	$C_{33}H_{31}O_6P$	71.47 (71.41)	5.63 (5.49)	1264	1216, 943	2.05, 10.47
10d	59	199–201	$C_{33}H_{31}O_6P$	71.47 (71.35)	5.63 (5.53)	1267	1218, 949	1.98, 10.51
11a	64	179–180	$C_{32}H_{29}O_6P$	71.01 (71.13)	5.23 (5.39)	1269	1209, 951	2.10, 7.26
11b	59	172–174	$C_{32}H_{29}O_6P$	71.01 (71.07)	5.23 (5.28)	1261	1212, 947	–, 7.21
11c	66	165–167	$C_{34}H_{33}O_6P$	71.70 (71.78)	5.68 (5.62)	1274	1218, 953	1.18, 4.21
11d	61	169–170	$C_{34}H_{33}O_6P$	71.70 (71.82)	5.68 (5.55)	1277	1219, 953	1.01, 4.12
12a	62	162–165	$C_{23}H_{21}Cl_2O_6PS$	52.38 (52.31)	4.01 (4.18)	1273	1215, 956	3.98, 8.36
12b	57	167–169	$C_{23}H_{21}Cl_2O_6PS$	52.38 (52.39)	4.01 (4.24)	1265	1210, 962	3.69, 8.54
12c	59	164–166	$C_{25}H_{25}Cl_2O_6SP$	57.24 (57.33)	4.69 (4.75)	1283	1213, 955	4.97, 10.02
12d	65	157–158	$C_{25}H_{25}Cl_2O_6SP$	57.24 (57.38)	4.69 (4.81)	1289	1216, 948	5.21, 9.20

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Table 2 ^{1}H NMR chemical shifts (J in Hz) of phosphorus and oxygen macroheterocycles (**10a–d**, **11a–d** and **12a–d**)

Compd	Aromatic	Methylene					Methyl
		P(O)–CH_2	(Ar)–O–CH_2	Central–CH_2	Bridged–CH_2		
10a	7.04–7.85 (m, 16H)	4.64–4.68 (m, 4H)	3.45–3.50 (m, 4H)	–	–	–	2.30 (s, 3H)
10b	6.99–7.80 (m, 16H)	4.61–4.66 (m, 4H)	3.49–3.55 (m, 4H)	–	–	–	2.28 (s, 3H)
10c	7.01–7.82 (m, 16H)	4.57–4.63 (m, 4H)	3.43–3.52 (m, 4H)	2.29– 2.36 (m, 4H)	–	–	2.28 (s, 3H)
10d	6.97–7.82 (m, 16H)	4.41–4.45 (m, 4H)	3.30–3.35 (m, 4H)	2.31–2.40 (m, 4H)	–	–	2.26 (s, 3H)
11a	7.01–7.74 (m, 16H)	4.38–4.42 (m, 4H)	3.62–3.65 (m, 4H)	–	5.14 (d, J = 15.8)	4.80 (d, J = 16.1)	2.32 (s, 3H)
11b	6.87–7.73 (m, 16H)	4.35–4.40 (m, 4H)	3.59–3.64 (m, 4H)	–	5.15 (d, J = 15.8)	4.82 (d, 16.0)	3.32 (s, 3H)
11c	6.94–7.79 (m, 16H)	4.39–4.43 (m, 4H)	3.54–3.60 (m, 4H)	2.27 (m, 4H)	5.17 (d, J = 15.9)	4.83 (d, J = 15.9)	3.28 (s, 3H)
11d	7.03–7.71 (m, 16H)	4.28–4.31 (m, 4H)	3.43–3.48 (m, 4H)	2.23–2.30 (m, 4H)	5.20 (d, J = 16.1)	4.72 (d, J = 16.1)	2.29 (s, 3H)
12a	6.83–7.58 (m, 16H)	4.34–4.39 (m, 4H)	3.48–3.52 (m, 4H)	–	–	–	2.25 (s, 3H)
12b	6.85–7.62 (m, 16H)	4.29–4.35 (m, 4H)	3.43–3.48 (m, 4H)	–	–	–	2.29 (s, 3H)
12c	6.92–7.75 (m, 16H)	4.32–4.36 (m, 4H)	3.41–3.45 (m, 4H)	2.31–2.37 (m, 4H)	–	–	2.24 (s, 3H)
12d	7.00–7.69 (m, 10H)	4.33–4.36 (m, 4H)	3.39–3.43 (m, 4H)	2.28–2.35 (m, 4H)	–	–	2.24 (s, 3H)

Table 3 ^{13}C NMR chemical shifts of **10a–d**, **11a–d** and **12a–d**

Compd	Carbon 1	Carbon 2	Carbon 3	Carbon 4	Carbon 5	Carbon 6	Carbon 7
10a	125.92 (C_1 & C_{19})	127.53 (C_2 & C_{18})	126.87 (C_3 & C_{17})	128.56 (C_4 & C_{16})	135.48 (C_{4a} & C_{15a})	115.32 (C_6 & C_{14})	154.35 (C_{6a} & C_{13a})
11d	127.81 (C_1 & C_{21})	124.48 (C_2 & C_{20})	122.65 (C_3 & C_{19})	128.37 (C_4 & C_{18})	131.56 (C_{4a} & C_{17a})	129.43 (C_5 & C_{17})	112.32 (C_6 & C_{16})
12d	131.82 (C_1 & C_{17})	127.03 (C_2 & C_{16})	125.32 (C_3 & C_{15})	113.19 (C_4 & C_{14})	143.95 (C_{4a} & C_{13a})	113.43 (C_{17a} & C_{18a})	54.52 (C_6 & C_{12})

Table 4 ^{13}C NMR chemical shifts of **10a–d**, **11a–d** and **12a–d**

Compd	Carbon 8	Carbon 9	Carbon 10	Carbon 11	Carbon 12	Carbon 13	Carbon 14
10a	126.58 (C_{19a} & C_{19d})	125.87 (C_{19b} & C_{19c})	53.29 (C_8 & C_{12})	55.82 (C_9 & C_{11})	142.34 ($C_{1'}$)	115.02 ($C_{2'}$)	125.82 ($C_{3'}$)
11d	151.92 (C_{6a} & C_{15a})	123.46 (C_{22a} & C_{22b})	26.35 (C_{22})	124.48 (C_1 & C_{21})	122.65 (C_1 & C_{21})	54.43 (C_8 & C_{14})	29.74 (C_9 & C_{13})
12d	29.31 (C_7 & C_{11})	56.18 (C_8 & C_{10})	149.54 ($C_{1'}$)	114.87 ($C_{2'}$ & $C_{6'}$)	129.37 ($C_{3'}$ & $C_{5'}$)	132.24 ($C_{4'}$)	19.87 4′ – CH_3

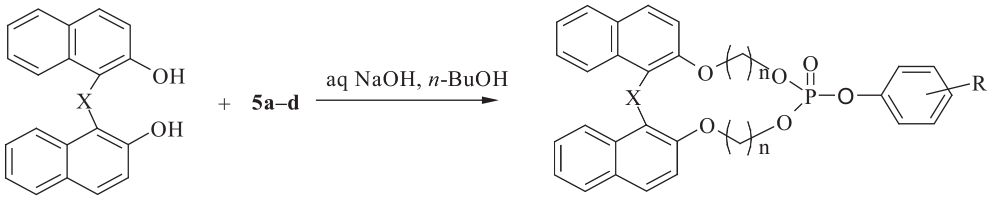
Table 5 ^{13}C NMR chemical shifts of **10a–d**, **11a–d** and **12a–d**

Compd	Carbon 15	Carbon 16	Carbon 17	Carbon 18	Carbon 19	Carbon 20
10a	126.12 ($C_{4'}$)	129.36 ($C_{5'}$)	127.54 ($C_{6'}$)	18.94 (6' – CH_3)	–	–
11d	55.54 (C_{10} & C_{12})	149.52 ($C_{1'}$)	114.46 ($C_{2'}$ & $C_{6'}$)	131.82 ($C_{3'}$ & $C_{5'}$)	129.58 ($C_{4'}$)	20.48 (4' – CH_3)
12d	–	–	–	–	–	–

Table 6 Mass spectral data of important ions of **10a**, **11d** and **12d**

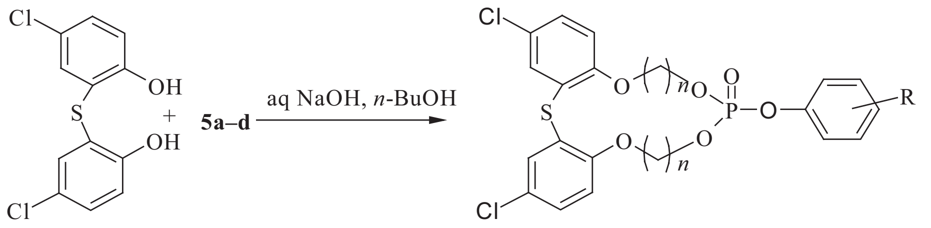
Compd	*m/z* (relative abundance)
10a	(M^+ + H, 527) (7), 396 (25), 361 (2), 327 (13), 297 (8), 281 (100), 265 (9), 252 (38), 239 (24), 205 (10), 149 (13), 141(17), 126(6), 113(8).
11d	(M^+ + H, 569) (11), 438 (30), 403 (23), 389 (18), 375 (12), 345 (18), 331 (10), 295 (60), 267 (21), 266 (41), 253 (100), 252 (34), 126 (53).
12d	(M^+ + H, 557) (9), 542 (30), 466 (18), 450 (24), 422 (11), 408 (7), 370 (30), 317 (5), 283 (100), 252 (35), 220 (44).

(1, 2) **(5a–d)**



(7–8) **(10a–d,11a–d)**

Compd	X	R	*n*
10a	–	2-CH_3	2
10b	–	4-CH_3	2
10c	–	2-CH_3	3
10d	–	4-CH_3	3
11a	CH_2	2-CH_3	2
11b	CH_2	4-CH_3	2
11c	CH_2	2-CH_3	3
11d	CH_2	4-CH_3	3



(9) **(12a–d)**

Compd	R	*n*
12a	2–CH_3	2
12b	4–CH_3	2
12c	2–CH_3	3
12d	4–CH_3	3

[M-$C_{21}H_{21}O_6P$] at *m/z* 126 confirming their macroheterocyclic structure.

In summary a simple synthesis for phosphorus and oxygen macroheterocycles (**10a–d, 11a–d, 12a–d**) by the reactants bis(2/3-chloroalkyl)phenyl triester of phosphoric acid (**5a–d**) with 2,2'-dihydroxybinaphthyl (**7**), bis(2-hydroxy-1-napthyl)methane (**8**), 5,5'-dichloro-2,2'-dihydroxybiphenyl sulfide (**9**) is reported.

Experimental

All reactions were carried out under anhydrous conditions in nitrogen atmosphere. Melting points were determined with open capillary tubes using Mel-temp apparatus. IR spectra (ν_{max} cm⁻¹) were recorded on a Perkin-Elmer 238 as KBr pellets. The ^1H, ^{13}C and ^{31}P NMR spectra were taken on Bruker AMX-400 MHz spectrometer operating at 400 MHz for ^1H, 100 MHz for ^{13}C and 161.9 MHz for ^{31}P. All the compounds were dissolved in $CDCl_3$ and chemical shifts were referenced to TMS (^1H and ^{13}C) and 85% H_3PO_4 (^{31}P). Mass spectra were collected on a GC–MS instrument at 70 eV. Elemental analysis were performed at the Central Drug Research Institute (CDRI), Lucknow, India. 2,2'-dihydroxybinaphthyl[20] (**7**), bis(2-hydroxy-1-napthyl)methane[21] (**8**), 5,5'-dichloro-2,2'-dihydroxybiphenyl sulfide[21] (**9**) were prepared according to reported procedures.

Synthesis of phosphorus and oxygen macroheterocyclic compound (**10a**): A solution of 2-methylphenyl phosphorodichloridate(**1**) (2.25 g, 0.01 mole) in 20 ml of dry toluene was added over a period of 20 min at 0°C, to a stirred solution of 2-chloroethanol (**3**) (1.6 g, 0.02 mole) and TEA (2.02 g, 0.02 mole) in 30 ml of dry toluene. After completion of the addition the reaction mixture was kept at room temperature and the reaction was stirred for another one and half hours. The progress of the reaction was monitored by TLC analysis on SiO_2 plate ethyl acetate and hexane, (1: 3) as eluents. The precipitated triethylamine hydrochloride was separated by filtration. The filtrate was rotaevaporated. The crude product obtained was dissolved in 5 ml of *n*-BuOH it was added over a period of 20 min to a boiling solution of 2,2'-dihydroxybinaphthyl (**7**) (2.28 g, 0.01 mole) and NaOH (0.8 g, 0.02 mole) in 30 ml of *n*-BuOH containing 2.30 ml of water. The reaction mixture was refluxed for an additional 6 h to complete the reaction as indicated by TLC analysis. The solvent was evaporated and the residue was column chromatographed (neutral silicagel as adsorbent, ethyl acetate-hexane (1 : 15) as eluent to give **10a**.

Synthesis of the other compounds **10b–d**, **11a–d, 12a–d** was achieved by the above procedure.

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