One-pot synthesis of new macroheterocyclic phosphoranes

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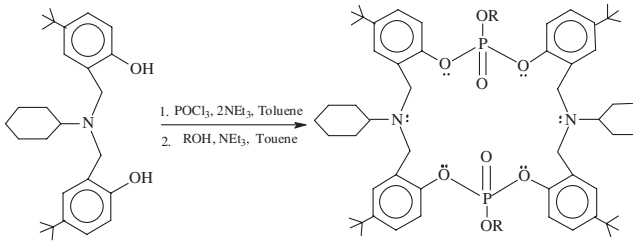
Synthesis of new macroheterocyclic phosphoranes (**2a–j**) was achieved by one-pot reaction of equimolar quantities of N,N-bis-(5-*t*-butyl-2-hydroxy-benzyl) cyclohexylamine (**1**), $POCl_3$ and various substituted phenols in the presence of NEt_3 in toluene at room temperature with stirring for 1 to 3 days under nitrogen. Their chemical structures were established by analytical and spectroscopic data.

Keywords: macroheterocyclic phosphoranes, aryloxyphosphoranes, N,N-bis-(5-*t*-butyl-2-hydroxybenzyl)cyclohexylamine

A number of methods for the synthesis of phosphorus macrocycles have recently been developed.[1-7] There has been interest in the chemistry of macrocycles containing both P(V) and P(III) atoms in view of their unique structures, reactivities and complexation abilities.[8-12] This makes them attractive not only for metal extraction from aqueous solution, but also as potential ligands for transition metal catalysed reactions in organic synthesis. Some functionalised phosphorus macrocycles have already found industrial and biological applications.[13-16] In this paper, we report a synthesis of novel aryloxy- and N,N-bis-(5-*t*-butyl-2-hydroxybenzyl)-cyclohexylamine[17] substituted macroheterocyclic phosphoranes (**2a–j**).

Aryloxy macroheterocyclic phosphoranes (**2a–j**) were prepared from N,N-bis-(5-*t*-butyl-2-hydroxybenzyl)cyclohexylamine (**1**). The reaction of 1 with $POCl_3$ and various arylphenols in the presence of triethylamine (TEA) in toluene at room temperature by using high dilution conditions afforded **2a–j** (Scheme 1). All compounds **2a–j** exhibited characteristic IR absorptions[18-19] (Table 1) for P=O, P–O–C_{ar} and N–C groups. The aromatic protons showed complex multiplets in the region δ 6.67–7.72. The singlet integrating for 36H in the region δ 1.24–1.27 is assigned to the *t*-butyl protons. The multiplets at δ 1.36–1.78, δ 3.56–4.24, are attributed to the cyclohexyl protons and methylene protons, respectively.[20] Other proton resonances appeared in the expected region[21] (Table 2).

The ^{13}C NMR chemical shifts[17,21] (Tables 3 and 4) were assigned by comparison with carbon chemicals shifts of **1** and related systems. The macroheterocyclic system (**2a–j**) showed nine signals for the N,N-Bis-(5-*t*-butyl-2-hydroxybenzyl) carbon atoms because of the symmetry of the system. Their ^{31}P NMR signals[6,22] (Table 1) appeared in the range of 2.01–6.92 ppm.



(**1**) (**2a-j**)

Compd.	R	Compd.	R
5a	4'-CH_3-C_6H_4	**5f**	C_6H_5
5b	4'-Cl-C_6H_4	**5g**	2',3'-$(CH_3)_2C_6H_3$
5c	2'-COOEt-C_6H_4	**5h**	2',4'-$(CH_3)_2C_6H_3$
5d	$C_{10}H_7$	**5i**	4'-(CH_3O)-C_6H_4
5e	4'-NO_2-C_6H_4	**5j**	2'-Cl-C_6H_4

Scheme 1

The GC–MS for **2a–j** data is given in Table 5. Appearance of $M^{+\bullet}$ at the appropriate molecular weights, $[M-(^{\bullet}OR)_2]^+$ at *m/z*

Table 1 Physical, IR and ^{31}P spectral data of aryloxy macroheterocyclic phosphoranes **(2a–j)**

Compd.	Yield /%	M.P /°C	Formula (M. wt)	(Calcd / Found)			IR cm^{-1} P=O	IR cm^{-1} P–O–C(Ar)	IR cm^{-1} >N–C	^{31}P NMR (δ)
2a	20	178–180	$C_{70}H_{92}O_8N_2P_2$	C, 73.04 (72.82)	H 8.0 (7.91)	O, 11.13 (11.00)	1262	1214, 911	1088	1.0, –3.06
2b	23	210–212	$C_{68}H_{86}O_8N_2Cl_2P_2$	C, 68.51 (68.32)	H, 7.22 (7.12)	O, 10.74 (10.56)	1261	1222, 943	1084	1.14, –2.93, –6.92
2c	14	205–206	$C_{74}H_{96}O_{12}N_2P_2$	C, 70.14 (70.01)	H, 7.58 (7.36)	O, 15.16 (15.03)	1248	1211, 908	1081	1.12, –2.84, –5.72
2d	16	162–164	$C_{76}H_{92}O_8N_2P_2$	C, 74.63 (74.68)	H, 7.52 (7.43)	O, 10.47 (10.34)	1264	1223, 915	1088	1.46, –2.9, –7.02
2e	21	216–218	$C_{68}H_{86}O_{12}N_4P_2$	C, 67.32 (67.18)	H, 7.09 (6.92)	O, 15.84 (15.71)	1265	1221, 927	1078	2.01, –2.73, –6.56
2f	18	156–158	$C_{68}H_{88}O_8N_2P_2$	C, 72.72 (72.61)	H, 7.84 (7.63)	O, 11.40 (11.24)	1253	1218, 921	1075	0.92, –2.64, –5.89
2g	24	161–162	$C_{72}H_{96}O_8N_2P_2$	C, 73.34 (73.20)	H, 8.14 (8.02)	O, 10.86 (10.68)	1261	1224, 918	1086	1.31, –2.63, –4.96
2h	29	183–185	$C_{72}H_{96}O_8N_2P_2$	C, 73.34 (73.18)	H, 8.14 (8.10)	O, 10.86 (10.71)	1260	1223, 918	1085	1.36, –2.81, –6.43
2i	31	154–155	$C_{70}H_{92}O_{10}N_2P_2$	C, 71.06 (69.94)	H,7.78 (7.83)	O, 13.53 (13.40)	1256	1218, 913	1080	1.24, –2.94, –5.86
2j	17	167–169	$C_{68}H_{86}O_8N_2Cl_2P_2$	C, 68.51 (68.39)	H, 7.22 (7.35)	O, 10.74 (10.61)	1264	1222, 915	1084	1.20, –2.71, –6.21

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Table 2 ^{1}H NMR chemical shifts (*J* in Hz) of **2a–j**

Compd.	*t*-butyl	Cyclohexyl	Methylene	Aromatic	Aryloxy substituents
2a	1.27 (s, 36H)	1.4–1.78 (m, 22H),	3.92–4.17 (m, 8H)	6.85–7.3 (m, 20H)	2.31 (s, 6H, CH_3)
2b	1.25 (s, 36H)	1.38–1.69 (m, 22H)	3.67–4.09 (m, 8H)	6.81–7.51 (m, 20H)	–
2c	1.25 (s, 36H)	1.36–1.70 (m, 22H)	3.56–4.12 (m, 8H)	6.72–7.61 (m, 20H)	4.28 (q,2H,OCH_2), 1.16 (t, 3H, CH_3)
2d	1.26 (s, 36H)	1.36–1.68 (m, 22H)	3.60–4.21(m, 8H)	6.67–7.42 (m, 26H)	–
2e	1.29 (s, 36H)	1.39–1.76 (m, 22H)	3.86–4.23 (m, 8H)	6.76–7.48 (m, 20H)	–
2f	1.24 (s, 36H)	1.38–1.72 (m, 22H)	3.90–4.21 (m, 8H)	6.74–7.56 (m, 22H)	–
2g	1.26 (s, 36H)	1.35–1.67 (m,22H)	3.85–4.06 (m, 8H)	6.78–7.38 (m, 18H)	2.34 (s, 3H, CH_3), 2.26 (s, 3H, CH_3)
2h	1.26 (s, 36H)	1.41–1.77 (m, 22H)	3.78–4.19 (m, 8H)	6.82–7.54 (m, 18H)	2.32 (s, 3H, CH_3) 2.24 (s, 3H, CH_3)
2i	1.27 (s, 36H)	1.40–1.73 (m, 22H)	3.84–4.24 (m, 8H)	6.8–7.64 (m, 20H)	3.70 (s, 3H, OCH_3)
2j	1.25 (s, 36H)	1.37–1.72(m, 22H)	3.76–4.11 (m, 8H)	6.71–7.72 (m, 20H)	–

Table 3 ^{13}C NMR chemical shifts of **2a–j**

Compd.	C_1 and C_{15}	C_2 and C_{14}	C_3 and C_{13}	C_4 and C_{12}	C_5 and C_{11}	C_6 and C_{10}	C_7 and C_9	C_{16}	C_{17}
2a	148.1	115.3	130.0	147.5	124.0	120.9	46.0	34.02	31.38
2b	149.7	115.7	127.8	147.4	125.1	122.7	45.9	34.1	31.1
2c	148.3	117.2	128.9	147.4	124.1	121.8	46.7	34.2	31.26
2e	147.8	118.4	128.3	147.3	124.5	120.6	46.4	34.06	31.1
2f	149.2	118.2	129.7	147.6	125.6	121.3	47.1	34.07	31.3
2g	149.8	117.2	129.1	147.2	126.2	121.7	45.4	34.11	31.36
2h	148.6	116.8	127.6	146.8	125.4	122.0	44.9	34.13	30.8
2i	148.5	115.5	131.4	147.5	124.3	122.3	45.3	33.9	31.0
2j	149.4	117.3	127.5	146.3	124.6	121.7	46.2	34.0	31.2

Table 4 ^{13}C NMR chemical shifts of **2a–j**

Compd.	C_1'	C_2' and C_6'	C_3' and C_5'	C_4'	C_1"	C_2" and C_6"	C_3" and C_5"	C_4"	Substitution
2a	153.7	121.3	128.8	134.9	55.6	27.9	26.6	25.2	20.7 (CH3)
2b	153.7	121.9	128.8	130.0	51.2	26.9	26.2	24.9	–
2c	152.8	118.8 128.3	132.6 131.0	119.2	54.3	26.6	26.6	23.9	C=O, 162.4, 64.2 (OCH2), 14.3 (CH3)
2d	–	–	–	–	–	–	–	–	–
2e	153.1	128.4	129.1 128.8	142.5	55.5	26.4	26.4	23.8	–
2f	152.3	122.1	127.8	125.1	55.3	27.8	25.8	25.6	–
2g	152.6	126.8 119.6	138.5 127.5	125.7	53.8	27.5	25.4	24.7	17.8 (2,3-CH3)
2h	152.3	127.3 119.4	128.5 126.2	133.6	54.6	28.2	27.0	25.0	16.7 (2,4-CH3)
2i	151.7	122.3	128.7	153.8	55.7	27.3	26.4	25.1	–
2j	152.6	121.8	128.7	131.6	54.5	27.8	26.5	25.7	57.2 (OCH_3)

Table 5 Mass spectral data of important ions of **2a** and **2b** *m/z* (relative abundance)

Compd.	*m/z* (relative abundance)
2a	(M^+, 115) (25), 1107 (32),982 (41), 970 (18), 936 (51), 926 (62), 850 (14), 768 (43), 712 (23), 578 (37) 544 (84), 418 (34), 423 (28), 188 (16), 280 (57), 265 (40)
2b	(M^+ + (1191) (30), (M^{+2}, 1193) (13), (M^{+4}, 1195) (6), 1119 (34), 1023 (62), 968 (57), 936 (42), 850 (20), 799 (17), 768 (28), 712 (31), 652 (280), 578 (25), 544 (80), 209 (51), 147 (18), 259 (37), 423 (71), 208 (33), 190 (22), 176 (18)

936, $[M-(C_6H_{12})_2]^+$ at *m/z* 768 $[M-(C_4H_8)_4]^+$ at *m/z* 712 and $[M-(C_6H_{12})\ (C_4H_4)_4]^+$ at *m/z* 544 confirmed the proposed macroheterocyclic systems. These ions may be used as diagnostic daughter ions for these compounds permitting their identification and quantification in the eco/bio environmental.

In summary, we have reported a simple synthesis of the aryloxy N,N-bis (5-*t*-butyl-2-hydroxybenzyl)cyclohexylamine substituted macrohetero-cyclic phosphoranes.

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 ^{1}H, ^{13}C and ^{31}P NMR spectra were taken on Bruker AMX-400 MHz spectrometer operating at 400 MHz for ^{1}H, 100 MHz for ^{13}C and 161.9 MHz. All the compounds were dissolved in DMSO-d_6 and chemical shifts were referenced to TMS (^{1}H and ^{13}C) and 85% H_3PO_4 (^{31}P). Mass spectral data were collected on a GC–MS instrument at 70 eV. Elemental analysis were performed at the Central Drug Research Institute (CDRI), Lucknow, India. N,N-Bis-(5-*t*-buyl-2-hydroxybenzyl)cyclohexylamine (**1**) was prepared according to a reported procedure.[17]

The purity of materials was assessed by elemental analysis. ^{1}H, ^{13}C and ^{31}P NMR and TLC.

Synthesis of 2-(4-Methylphenoxy) macroheterocyclic phosphorane (**3a**): N,N-Bis-(5-t-butyl-2-hydroxybenzyl) cyclohexylamine (0.1 mole) was dissolved in toluene (500 ml) and phosphrous oxychloride (0.1 mole) was added under N_2, followed by slow addition with stirring of triethylamine (0.2 mole). After 1 h of additional stirring, a solution of 4-methylphenol (0.1 mol) and triethylamine (0.1 mol)

in toluene (50 ml) was added dropwise with constant stirring to the above crude acid chloride solution. After the addition, the mixture was stirred at room temperature for 3 days. Progress of the reaction was monitored by TLC. On completion of the reaction, the solid triethylamine hydrochloride was filtered off. The solution of reaction mixture was dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel (elution with ethyl acetate – hexane 2:5 v/v). Other members of **2** are prepared by this procedure. Physical and spectral data of **2a–j** are provided in Tables 1–5.

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