SYNTHESIS OF NEW CYCLOPHOSPHAZENES CONTAINING POLYOXYETHYLENE MOIETIES[1]

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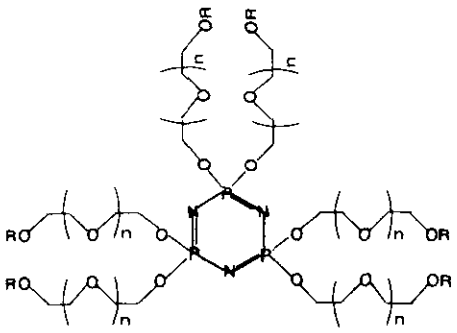
Abstract - Hexa-substituted cyclophosphazenes are formed by the reaction of hexachlorocyclophosphazenes with polyethylene glycols mono alkyl ether and employed as transfer catalysts in anion-promoted reactions.

Several examples of the use of cyclophosphazenes have been reported during the last years[2].

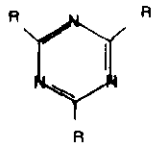
The cyclophosphazenic compounds have been reported to have ability to form clathrates with a wide range of solvents[2,3] and, moreover, some cyclophosphazenic systems containing either chlorine pairs or highly basic endocyclic nitrogen atoms have been studied and tested on a their potential anti-tumor activity[4].

Although various types of cyclophosphazenic derivatives have recently been designed and synthetized[5-8], no case on the synthesis of cyclophosphazenes containing armed acyclic poly ethers were reported in the literature.

Following our research in the field of macrocyclic chemistry[9], in the present paper the detailed results of synthesis of hexa-substituted cyclophosphazenes from hexachlorocyclophosphazene and oligoethylene glycols mono alkyl ether are described.



1a–d



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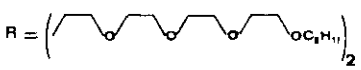

a) n = 1 R = $-C_4H_9$

b) n = 1 R = $-C_8H_{17}$

c) n = 2 R = $-C_4H_9$

d) n = 2 R = $-C_8H_{17}$

The compounds 1a-d were prepared by condensation of phosphonitrilic chloride trimer and sodium hydride with triethyleneglycol monoalkyl ether respectively in tetrahydrofuran (THF) refluxing for 48h. The reaction mixture was purified by column chromatography by silica gel to afford 1a-d as viscous liquids.

All compounds have been determined by their analytical and spectroscopic data which were in agremeent with the proposed structures.

The ir spectra of all compounds exhibit the characteristic band due to the $N{=}P{-}OCH_2$ group[10] at 1230-1220 cm^{-1}. The nmr spectra exhibit three group of signals as show in table 1.

These compounds can be employed as phase-transfer catalysts in anion-promoted reactions in a two-phase aqueous-organic system according to the method described by Montanari[11] and were compared with the polypode ligand 2 (see table 2).

The activity of 1a-d is high in the nucleophilic substitutions of bromide with iodide and of sodium thiophenate with 1-bromo-octane, in the alkylation of phenylacetone with 1-bromo-butane.

It is known that in the polypode ligands, catalytic acticity is maximum for compounds with six polyethylene branches, and diminishes when the terminal alkyl group is shortened or the number of branches is reduced[12].

The catalytic activites of 1a-d increase with the increase number of polyethy-

lene branches and are higher than those of the polypode ligand 2[12]. Therefore, these species of compounds can be used in phase-transfer catalyzed reactions.

Table 1: The physical costants and yields of hexa-substituted cyclophosphazenes[a] (1b-d)

Starting material n	R	Product	$n_D^{T/°C}$	Yield(%)	NMR ($CDCl_3$, δ)
1	$-C_8H_{17}$	1b	n_D^{25} 1.4644	18%	4.00-3.25 (m,60H), 1.76-1.01 (m, 72H), 0.85 (t,18H)
2	$-C_4H_9$	1c	n_D^{21} 1.4643	29%	4.04-3.25 (m, 84H), 1.68-1.09 (m, 24H), 0.86 (t,18H)
3	$-C_8H_{17}$	1d	n_D^{21} 1.4653	30%	4.13-3.23 (m, 84H), 1.60-1.00 (m,72H), 0.78 (t,18H)

a) IR spectra are almost the same as that of 1a. All the compounds reported here gave satisfactory elemental analyses.

Table 2: Influence of the catalysts on nucleophilic reactions carried out under phase-transfer conditions

Substrate[a]	Reagent[b]	Catalyst[e]	T/°C	Time/h	Yield%[f]	Product[g]
$n-C_8H_{17}Br$	KI	1a	80	8	68	$n-C_8H_{17}I$
"	"	1b	80	8	88	"
"	"	1c	80	2	79	"
"	"	1d	80	2	73	"
"	"	2	60	3	85	"
"	C_6H_5SNa[c]	1a	20	8	97	$C_6H_5SC_8H_{17}$
"	"	1b	20	8	98	"
"	"	1c	20	1	92	"

Table 2 cont'd

"	"	1d	20	1	81	"
"	"	2	20	5	70	"
$C_6H_5CH_2COCH_3$	$n\text{-}C_4H_9Br$[d]	1a	20	8	69	$C_6H_5CH(C_4H_9)COCH_3$
"	"	1b	20	8	94	"
"	"	1c	20	4	94	"
"	"	1d	20	4	88	"
"	"	2	20	4	78	"

[a]The reactions were carried out with a saturated aqueous solution of the reagent: no solvent was used for the substrate. [b]5 Mol. equiv. [c]1 Mol. equiv. [d]1.2 Mol. equiv. in 50% aq. NaOH. [e]0.05 Mol. equiv. [f]By g.l.c. analysis. [g]The products were characterized by g.l.c. retention time.

The synthesis of new cyclophosphazenes and a spectroscopic mass investigation on the mechanistic aspects of the fragmentation of compounds 1a-d will be reported in a future work.

EXPERIMENTAL

IR spectra were recorded with a Perkin-Elmer 157G spectrophotometer; nmr spectra were determined with a Varian EM 360 L spectrometer (TMS as internal reference). Microanalyses for CHN were carried out on a Carlo Erba model 1106 Elemental Analyzer. The reactions under phase-transfer conditions were carried out on a Carlo Erba model HRGL 5300 gas-chromatography (SE 30, 3% on Chromosorb or Carbowax 20M.).

Material starting

Tetrahydrofuran (THF) was distilled over $LiAlH_4$ under an atmosphere of dry nitrogen and immediately used.
Diethylene glycol, triethylene glycol, diethylene glycol mono-butil ether, triethylene glycol mono-butil ether, dihydropyran, octil bromide were used

without further purification.

Diethylene glycol mono-octyl ether, triethylene glycol mono-octyl ether and polypode ligand 2.

The preparation of these was carried out according to the literature procedures[12].

General method for the preparation of compounds 1a-d

To a suspension of a rapidly stirred solution of the hexachlorocyclophosphazene (5 gr, 0.014 mol) and sodium hydride (8 gr, 0.33 mol) in 75 ml of tetrahydrofuran was added dropwise a solution of polyoxyethylene glycol mono alkyl ether (23.3 gr, 0.14 mol) in 150 ml of tetrahydrofuran at room temperature over a period of 1h and then refluxed for 48h. The reaction mixture was filtered and the remained solid was washed with dichloromethane. Upon removing the solvent in reduced pressure from the combined solution, a viscous liquid was obtained and purified by column chromatography by silica gel, chloroform-methanol (10:1) as eluent, to afford 1 as a viscous liquid.

Hexadiethylene glycol mono-buthyl ether-cyclophosphazene 1a

Yield: 26%, n_D^{21} 1.4601; ir (neat): 2940, 2860, 1460, 1360, 1230, 1220, 1060, 960, 860 cm^{-1}; nmr ($CDCl_3$): δ 4.06-3.20 (m, 60H, O-$\underline{CH_2}$-), 1.56-1.06 (m, 24H, $\underline{CH_2}$), 0.78 (t, 18H, -$\underline{CH_3}$).
Anal. Calcd. for $C_{48}H_{102}N_3O_{18}P_3$: C, 52.01; H, 9.27; N, 4.33. Found : C, 51.86; H, 9.35; N, 4.30.

Hexadiethylene glycol mono-octyl ether-cyclophosphazene 1b, hexatriethylene glycol mono-buthyl ether-cyclophosphazene 1c, hexatriethylene glycol mono-octyl ether-cyclophosphazene 1d.

The compounds 1b-d were prepared as described for 1a and the physical costans, yields and spectroscopic data were shown in table 1.

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