SYNTHESIS AND CHARACTERIZATION OF 6-SUBSTITUTED DIBENZO [d,f][1,3,2] DIOXA PHOSPHEPIN 6-OXIDES

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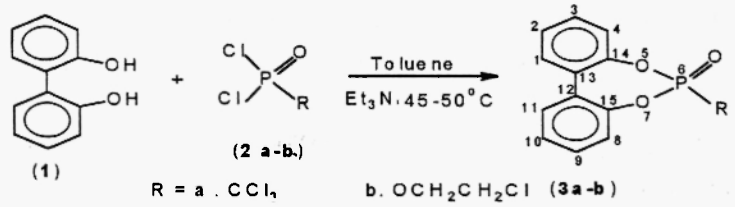
Abstract : Several 6-trichloromethyl dibenzo[d,f] [1,3,2] dioxaphosphepin 6-oxide (3a), 2-chloroethoxy dibenzo[d,f] [1,3,2] dioxaphosphepin 6-oxide (3b) and alkylcarbamato dibenzo [d,f] [1,3,2] dioxaphosphepin 6-oxides (6a-c) have been synthesized from reactions of equimolar quantities of 2,2'-dihydroxybiphenyl (1) with trichloromethylphosphonic dichloride (2a), O-2-chloroethyl phosphoryldichloride (2b) and dichlorophosphinyl carbamates (5a-c) at 45-50°C for (3a & 3b) and 40-45°C for (6a-c) in dry toluene in the presence of triethylamme. Elemental, IR and NMR (^1H & ^{31}P) data have been discussed and supported all structures.

Introduction

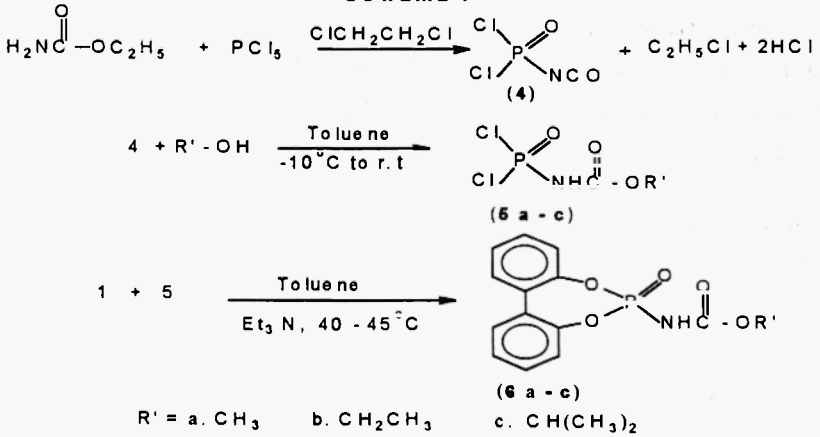
A variety of organophosphorus compounds containing 1,3,2-dioxaphospholene and 1,3,2-dioxaphosphorinane have been used in cancer chemotheraphy[1,2] and those of dibenzo[d,f] [1,3,2] dioxaphosphepins as stabilizers in polymer field[3]. Certain phosphorus carbamates possess antitumour, anticarcinogenic, pesticidal and bactericidal properties[2,4-8]. In view of their diverse applications, we have synthesized novel 6-trichloromethyl / chloroethoxy / alkylcarbamato dibenzo [d,f] [1,3,2] dioxaphosphepin 6-oxides and characterized them by elemental, IR and NMR (^1H & ^{31}P) spectral analyses.

Results and Discussion

When equimolar quantities of 2,2'-dihydroxybiphenyl (1) were condensed with trichloromethyl phosphonicdichloride (2a), O-2-chloroethylphosphoryldichloride (2b) and dichloroisocyanatophosphinyl carbamates (5a-c),members of 3 and 6 were obtained (Scheme 1 & 2). The dichloroisocyanato phsophinyl carbamates (5a-c) have been obtained by the nucleophilic addition reaction of various dry alcohols to isocyanatophosphonic dichloride (4) at -10°C in dry toluene (scheme 2). Two equivalents of triethylamine as the base in dry toluene as the solvent and with



SCHEME 1



SCHEME 2

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temperature ranging between 45-50°C for (3a & 3b) and 40-45°C for (6a-c) was found to be ideal to effect this cyclocondensations. Physical and spectral data of the compounds are found in tables 1-2.

The IR spectra[9] of 3 a and 3b showed bands (in cm^{-1}) at 1302 and 1297 respectively for (P=O) and 3b also exhibited band at 1030 for P-O-($C_{aliphatic}$). Compounds 6 a-c showed bands in the region 1247 1284 (P=O), 1743-1746 (C=O) and 3214-3271 (PN-H) (Table 1). Proton NMR spectra [10] were simple for these systems.

The protons of aromatic moieties showed multiplets in the range of δ 7.19-7.52 for 3a and δ 7.18-7.65 for 3b, while on the chloroethyl group in 3b appeared as triplets at δ 4.39 and δ 3.66 for OCH_2 and CH_2Cl groups respectively. Similarly the aromatic protons in 6 a-c appeared as complex multiplets in the range of δ 7.22-7.61 (Table 2). The P-NH proton of the carbamate moiety in compounds 6 a-c resonated as doublets in the region δ 6.03-6.67 ($^2J_{P-NH}$=14.8 Hz). It is interesting to note that the coupling is limited to P-NH only and not extended to the other protons of the carbamate moiety. It is also observed that the signals for the protons of the carbamate function appeared in slightly down field when compared to the signals of the corresponding protons in the free alcohols[11].

Phosphorus resonance signals in 3a were observed at δ 8.32 and compounds 6a-c exhibited signals in two regions at δ -0.37 to -4.19 and δ - 0.55 to 12.75. The two signals in ^{31}PNMR spectrum may be due to the presence of two conformers[12].

Experimental

All melting points were determined in open capillary tubes on a Mel-Temp apparatus and are uncorrected. IR spectra (δ_{max} in cm^{-1}) were recorded as KBr pellets using a Perkin-Elmer 1000 unit. The ^{1}H and ^{31}P NMR spectra were recorded in $CDCl_3$ using varian AMX-400 MHz instrument and chemical shifts were referenced to TMS (^{1}H) and 85% H_3PO_4 (^{31}P). Microanalytical data were obtained from Central Drug Research Institute, Lucknow, India.

Synthesis of 6 - trichloromethyl dibenzo [d,f] [1,3,2] dioxaphosphepin 6- oxide (3a)

The general procedure to obtain the compounds 3a and 3b is illustrated for the preparation of 3a. A solution of trichloromethyl phosphonicdichloridate (2a, 2.36 g, 0.01 mol) in dry toluene (25 mL) was added dropwise to a stirred solution of 2,2'-dihydroxybiphenyl (1, 1.86 g, 0.01 mol) and triethylamine (2.02 g, 0.02 mol) in dry toluene (60 mL) at 0°c. After the addition was complete, the temperature was slowly raised to 45-50°C and was then maintained for 5-6 hours with stirring. The completion of the reaction was monitored by TLC analyses. After cooling to room temperature, the triethylamine hydrochloride was filtered off, and the filtrate was evaporated under reduced pressure. The gummy residue was washed with water, dried and treated with 2-propanol. A white solid formed and was recrystallised from 2-propanol to afford 3a, yield 0.168 gr(48%), mp 134-136°C. Physical and spectral data for compounds 3a and 3b are given in tables 1-2.

Synthesis of 6 - ethylcarbamato dibenzo [d,f] [1,3,2] dioxaphosphepin 6-oxide (6b)

The general procedure for members of 6 is illustrated with that for 6b. A solution of ethanol (0.46 g, 0.01 mol) in dry toluene (20 mL) was added dropwise (20 min) to a cold (-10°C) solution of 4[5] (1.60 g, 0.01 mol) in dry toluene (20 mL). After the addition was complete, the reaction mixture was allowed to warm slowly to room temperature and stirring was continued for 2 hours. The new reaction mixture was then added dropwise to a cold (0°C)

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Table 1: Physical properties[a] and IR spectral(Cm^{-1}) data of compounds (3a-b & 6a-c)

Compd	Mol. Formula (Mol.wt)	M.P °C	Yield %	Found (Calcd)% C	H	IR(Cm^{-1}) C=O	P=O	P-NH
3a	$C_{11}H_8O_3Cl_3P$ (349.53)	134-136	48	44.51 (44.67)	2.27 (2.31)	-	1302	-
3b	$C_{14}H_{12}O_4ClP$ (310.67)	70-73	90	54.26 (54.12)	3.79 (3.84)	-	1297	1030 (P-O-($C_{aliphatic}$)
6a	$C_{14}H_{12}O_5NP$ (305.23)	245-248	52	54.91 (55.09)	4.11 (3.96)	1745	1247	3249
6b	$C_{15}H_{14}O_5NP$ (319.25)	250-252	60	56.52 (56.43)	4.39 (4.42)	1746	1248	3214
6c	$C_{16}H_{16}O_5NP$ (333.28)	177-180	57	57.48 (57.66)	4.89 4.84	1743	1284	3271

[a]Recrystalised from 2-Propanol

Table 2: ^1H and ^{31}P NMR data [a,b] of compounds 3a-b and 6a-c

Compd.	Ar-H	R-H	-NH	^{31}P NMR[c]
3a	7.19 - 7.52 (m. 8H)	-	-	8.32
3b	7.18 - 7.65 (m, 8H)	4.39 (t, 2H, OCH_2) 3.66 (t, 2H, CH_2Cl)	-	-
6a	7.27 - 7.58 (m, 8H)	3.64 (S, 3H, OCH_3)	6.67 (brs)	-0.43 12.73
6b	7.28 - 7.61 (m, 8H)	1.15 (t, 3H, CH_3) 4.10 (q, 2H, OCH_2)	6.22 (d,J=16Hz)	-0.37 12.76
6c	7.22-7.52 (m,8H)	4.77 -4.85 (m, 1H, OCH) 1.06-1.08 (m, 6H, $2CH_3$)	6.03 (d,J=13.6Hz)	-4.19 -0.55

[a]Chemical shifts in δ from TMS, J(Hz) given in parentheses
[b]Recorded in $CDCl_3$
[c]Chemical shifts in δ from 85% H_3PO_4

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solution of 1 (1.86 g, 0.01 mol) and triethylamine (2.02 g, 0.02 mol) in dry toluene (50 mL). When the addition was complete, the mixture was stirred and allowed to warm slowly to 40-45^{0}C and maintained at this temperature for 7 hours. The completion of the reaction was monitored by TLC analysis. The solid triethylamine hydrochloride was filtered off and the solvent was evaporated under reduced pressure. The gummy residue was washed with water, dried and treated with 2-propanol. A white solid obtained after recrystallization of the crude product from 2-propanol afforded 6b, yield 0.192 g (60%), mp 250-252^{0}C. Physical and spectral data of 6a-c are given in tables 1-2.

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