Preparation, Infrared and Mass Spectral Studies of 6-Substituted 6,7-Dihydro-5*H*-dibenzo[*d*,*f*][1,3,2]diazaphosphepine 6-Oxides

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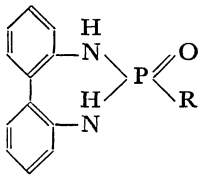
Several 6-substituted 6,7-dihydro-5*H*-dibenzo[*d*,*f*][1,3,2]diazaphosphepine 6-oxides have been synthesized and their structures were confirmed by IR and mass spectra. The existence of hydrogen bonding between the amidic hydrogens and the phosphoryl oxygen in theses compounds is indicated by the IR spectra. Under electron impact, the splitting pattern of these compounds takes about four major fragmentation pathways. The stability of dibenzodiazaphospheine cyclic system is indicated by the appearence of ions at *m/e* 229 and 211 corresponding to the species $C_{12}H_{10}N_2OP^+$ and $C_{12}H_8N_2P^+$, respectively, in all the spectra of the compounds except in the methyl and ethyl substituted compounds.

Considerable interest in organophosphorus compounds has been sustained by medical and commercial applications of their biological properties. The syntheses of these compounds containing benzodiazaphosphole ring have acquired much importance recently as these compounds have been investigated for their insecticidal, bactericidal, antiviral and anticarcinogenic properties.[1] The search for a satisfactory drug for cancer produced many new phosphorus heterocyclic compounds[2–5] and many of them possessed significant antitumour activity. These laboratories have reported[6] earlier the synthesis of several 2-(4-chloro-3-methylphenoxy)-2,3-dihydro-1*H*-1,3,2-benzodiazaphosphole 2-oxides, and the present paper describes the synthesis, infrared and mass spectral studies of 6-substituted 6,7-dihydro-5*H*-dibenzo[*d*,*f*][1,3,2]diazaphosphepine 6-oxides (**1**—**8**).



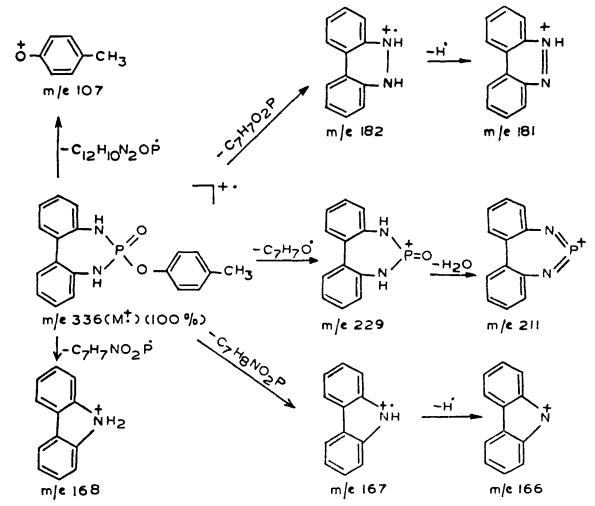
R	R
1 CH_3	**5** C_6H_5
2 C_2H_5	**6** O-$C_6H_4CH_3$(*p*-)
3 $(CH_2)_2CH_3$	**7** O-$C_6H_4NO_2$(*p*-)
4 $CH(CH_3)_2$	**8** O-$C_6H_3ClCH_3$(4,3-)

These cyclizations were accomplished by reacting equimolar quantities of various phosphonic dichlorides and phosphorodichloridates with 2,2′-diaminobiphenyl in refluxing benzene or toluene under nitrogen atmosphere. The yields of diazaphosphepines obtained (see Table 1) indicate that nucleophilic substitution of the amino groups proceeds more easily leading to the completion of cyclization with phosphorodichloridates than with phosphonic dichlorides. This may be explained by the fact that substituted phenoxyl groups attached to the phosphorus atom renders it more electrophilic. The lowest yield is obtained in the case of methylphosphonic dichloride. This may be due to the electron donating effect of methyl group by hyperconjugation which renders the phosphorus atom of the dichloride less electrophilic. All these compounds are crystalline solids with high melting points and are also easily soluble in organic solvents. They appear to be more stable than benzodiazaphosphole 2-oxides.[6]

The infrared frequencies associated with the major functional groups of the compounds in the present investigation are plotted in Table 2. All the compounds have exhibited P=O and P–NH vibrations in the regions 1210—1140 cm^{-1} and 3400—3080 cm^{-1}. The free P=O and NH stretching vibrations would give rise to bands around 1300—1250 cm^{-1} and 3350—3210 cm^{-1} [7,8] respectively. Bellamy[8] has also assigned 1250—1150 cm^{-1} for P=O stretching vibrations in the compounds which involve hydrogen bonding. The frequencies exhibited by P=O and P–NH groups indicate that they have involved in the hydrogen bond formation. All the compounds exhibited characteristic infrared frequencies for P–O–C_{aryl}[9–13], P–N_{phenyl}[14], P–N[14], aryl C–NO_2[15–17] and aryl C–Cl[18] groups.

To confirm the configuration of the cyclic system present in these molecules and also to study the splitting patterns and fragmentation pathways of this system, the mass spectra of these compounds (**1**—**8**) have been studied. As a general representation of this series, the splitting pattern and the fragmentation pathways of (*p*-methylphenoxy)dibenzodiazaphosphepine (**6**) under electron impact are shown in Scheme 1 (Fig. 1). The molecular ion, $C_{19}H_{17}N_2O_2P^+$, (*m/e* 336) itself appears as the most abundant ion for this compound. The initial fragmentation of the molecular ion occurs by ejecting the C_7H_7O radical attached to the phosphorus atom with the formation of the ion $C_{12}H_{10}N_2OP^+$ at *m/e* 229 (20%). This ion loses a water molecule to form the ion, $C_{12}H_8N_2P^+$ at *m/e* 211 (15%).

The ions at *m/e* 182 (16%) and 181 (24%) corresponding to the species $C_{12}H_{10}N_2^+$ and $C_{12}H_9N_2^+$ might



Scheme 1.

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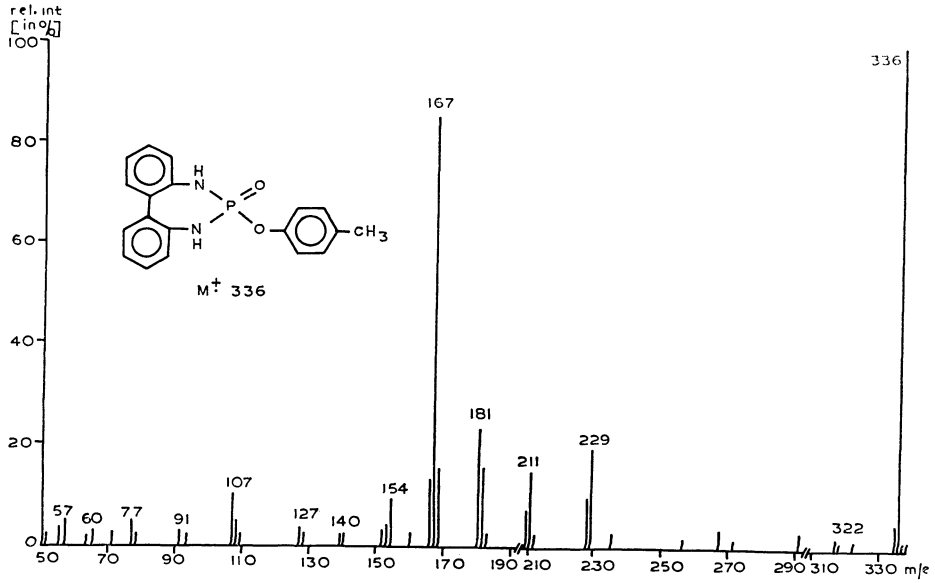

Fig. 1. Mass spectrum of 6-(4-methylphenoxy) 6,7-dihydro-5*H*-dibenzo[*d*,*f*][1,3,2]diazaphosphepine 6-oxide at 70 eV.

Table 1. Synthesis of 6-substituted 6,7-dihydro-5*H*-dibenzo[*d*,*f*][1,3,2]diazaphosphepine 6-oxides

Compound	Phosphonic dichloride or phosphorodichloridate	Yield (%)[a]	Reaction time (min)[b]	Mp (°C)	Molecular formula	Found (%) C	H	N	Calcd (%) C	H	N
	With 2,2′-diaminobiphenyl										
1	Methylphosphonic dichloride	47[c]	115	252—255[e]	$C_{13}H_{13}N_2OP$	63.78	5.41	11.32	63.93	5.36	11.48
2	Ethylphosphonic dichloride	58[c]	120	226—228[f]	$C_{14}H_{15}N_2OP$	65.02	5.94	10.82	65.10	5.85	10.85
3	Propylphosphonic dichloride	84[c]	120	225—228[g]	$C_{15}H_{17}N_2OP$	66.29	6.25	10.49	66.15	6.29	10.29
4	Isopropylphosphonic dichloride	68[c]	120	205—210[e]	$C_{15}H_{17}N_2OP$	66.08	6.35	10.19	66.15	6.29	10.29
5	Phenylphosphonic dichloride	89[c]	115	330—333[h]	$C_{18}H_{15}N_2OP$	70.71	5.27	8.95	70.60	4.94	9.15
6	*p*-Tolyl phosphorodichloridate	80[c]	120	255—257[h]	$C_{19}H_{17}N_2O_2P$	67.69	4.95	8.36	67.85	5.09	8.47
7	*p*-Nitrophenyl phosphorodichloridate	92[c]	120	255—257[i]	$C_{18}H_{14}N_3O_4P\frac{1}{2}H_2O$	57.38	4.00	10.94	57.46	4.02	11.12
8	4-Chloro-3-methylphenyl phosphorodichloridate	88[d]	120	234—238[i]	$C_{19}H_{16}N_2O_2ClP$	61.43	4.42	7.43	61.55	4.35	7.56

a) Product isolated after one crystallization. b) As the reagents were mixed at about 40—60 °C and then heated to reflux, the times recorded are approximate. Reactions were carried out in refluxing, c) benzene and d) toluene. Products recrystallized from e) methanol-ether, f) ethanol-ether, g) chlorobenzene, h) 95% ethanol, and i) methanol.

Table 2. Infrared spectra of 6-substituted 6,7-dihydro-5*H*-dibenzo[*d*,*f*][1,3,2]diazaphosphepine 6-oxides

Compound	P=O (cm^{-1})	P-NH (cm^{-1})	P-N-C aromatic: P-N-C (aryl) (cm^{-1})	P-N-C aromatic: P-N (cm^{-1})	*ortho*-Disubstituted benzenes (cm^{-1})	P-O-C aromatic (cm^{-1})		
1	1140	3250	1310	950	760	—		
2	1140	3375	1300	945	760	—		
3	1175	3150	1280	930	760	—		
4	1140	3400	1290	940	765	—		
5	1190	3080	1280	930	750	—		
6	1210	3150	1285	925	760	1220	950	
7	1205	3150	1285	935	758	1235	980	aryl C-NO_2 1510 cm^{-1} 1340 cm^{-1}
8	1160	3150	1280	938	755	1220	978	aryl C-Cl 1060 cm^{-1}

Table 3. Mass spectral data

Compound No.	*m/e* (% relative abundance)
1	181(100), 180(45), 179(12), 167(9), 166(39), 165(58), 164(23), 91(15).
2	182(24), 181(19), 180(81), 179(21), 167(17), 166(78), 165(100), 164(43), 139(12), 138(16), 92(13), 91(28), 90(70), 79(35), 77(16), 65(11), 51(11).
3	272(M^+, 50), 244(14), 230(62), 229(8), 213(22), 211(12), 182(17), 181(21), 180(10), 168(20), 167(100), 166(23), 93(16).
4	272(M^+, 14), 244(4), 184(79), 183(35), 182(8), 168(42), 167(59), 166(25), 138(11), 137(12), 129(10), 127(11), 126(10), 92(45), 91(100), 90(21), 89(24), 78(28), 77(58), 65(48), 64(23), 63(37), 52(30), 51(47).
5	307(13), 306(M^+, 62), 290(25), 211(4), 182(7), 181(11), 168(15), 167(100), 166(8), 153(19), 93(10), 67(11), 55(11).
7	367(M^+, 22), 337(18), 336(61), 292(10), 291(59), 229(21), 211(18), 182(20), 181(28), 168(20), 167(100), 166(18), 154(14), 153(41), 152(11), 114(15), 113(13), 109(22), 108(12), 107(18), 93(11), 91(11), 78(22), 77(14), 66(15), 64(25), 58(12), 57(13), 55(18), 51(8).
8	372(20), 371(14), 370(60), 229(33), 228(13), 211(19), 182(21), 181(26), 168(14), 167(100), 166(17), 154(11).

have been formed from the molecular ion by the cleavage of P–N bonds followed by the loss of hydrogen atom.

The ion at *m/e* 168 (16%) might have resulted by the loss of $C_7H_7NO_2P^{\cdot}$ from the molecular ion. In another mode of decomposition, the molecular ion might have lost $C_7H_8NO_2P$ resulting with the formation of a cation radical at *m/e* 167 (92%) corresponding to the species $C_{12}H_9N^+$. This ion on further loss of a hydrogen radical leads to the formation of the ion $C_{12}H_8N^+$ at *m/e* 166 (13%). The loss of $C_{12}H_{10}N_2OP^{\cdot}$ from the molecular ion by the rupture of the P–O bond results with the formation of the ion at *m/e* 107.

This general fragmentation pattern is observed for all other compounds in this series. The mass spectral data of the other compounds (**1**—**5**, **7**, and **8**) are presented in Table 3. An examination of all their spectra indicates that 6-aryl substituted compounds are more stable under electron impact than the 6-alkyl substituted compounds. The methyl and ethyl substituted dibenzodiazaphosphepines (**1** and **2**) do not show any peaks corresponding to their molecular ions. The mass spectra of **4**, **7**, and **8** show uniformly the ion at *m/e* 167 as their base peak. Even for **6** this ion appears with an intensity of 92 per cent.

The ions at *m/e* 229 and 211 corresponding to the species $C_{12}H_{10}N_2OP^+$ and $C_{12}H_8N_2P^+$ respectively (refer Scheme 1) are present as characteristic peaks in all the compounds except for methyl- and ethyl-substituted compounds (**1** and **2**). The ions at *m/e* 182 and 181 derived from the diamine fragment of the molecular ions are found to appear in the spectra of all the compounds.

Apart from these general peaks present in the spectra of all these molecules, the peaks can be explained as follows: the ion at *m/e* 337 in the spectrum of **7** might have been formed by the loss of NO from the NO_2 of the compound.[20] The ion at *m/e* 244 is observed in the spectra of both **3** and **4** and it might have been formed by the ejection of C_2H_4 from the alkyl substituents of their molecular ions.[21]

Experimental

All melting points were determined on a Mel-Temp apparatus and are uncorrected. The elemental analyses were performed by Dr. R. D. MacDonald, Australian Microanalytical Service. IR spectra were recorded on a Perkin-Elmer Model 700 in Nujol mulls. Mass spectra were determined using a Varian Mat CH7, electron energy 70 eV and trap current 100 μA at Indian Institute of Technology, Madras.

2,2′-Diaminobiphenyl. It was prepared by reduction of 2,2′-dinitrobiphenyl,[22] mp 78—79 °C (lit,[23] mp 77—78 °C).

Methyl-, ethyl-, propyl-, and isopropylphosphonic dichlorides were obtained from Speciality Organics, Inc., U. S. A. and phenylphosphonic dichloride was procured from Fluka. 4-Chloro-3-methylphenyl phosphorodichloridate[6], *p*-tolyl phosphorodichloridate,[6] *p*-nitrophenyl phosphorodichloridate[24] were prepared according to the procedures reported in the literature.

*6-Phenyl 6,7-Dihydro-5*H*-dibenzo*[d,f][*1,3,2*]*diazaphosphepine 6-Oxide (5).* A solution of phenylphosphonic dichloride (3.9g, 0.02 mol) in dry benzene (20 ml) was added drowise to a warm (40—50 °C) and stirred solution of 2,2′-diaminobiphenyl (3.7g 0.02 mol) in dry benzene (30 ml). A slow stream of nitrogen was bubbled through the reaction mixture and the progress of the condensation was followed by titrating the evolved HCl gas with standard alkali. The reaction mixture was brought to reflux temperature and the evolution of the calculated amount of HCl was complete in 95 min. The reaction mixture was refluxed with vigorous stirring for an additional 20 min and cooled. On working up, the reaction mixture yielded 5.4g (89%) of the product which on recrystallization from 95% ethanol four times afforded an analytical samples of 6-phenyl-6,7-dihydro-5*H*-dibenzo[*d,f*]-[1,3,2]diazaphosphepine 6-oxide (**5**), mp 330—333 °C (dec).

This typical procedure was used as a general method for the preparation of all other compounds (**1**—**4**, **6**—**8**) reported and their relevant details are summarized in Table 1.

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