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Synthesis and Characterization of N,N-Dimethylamino-N',N''-diarylamino Phosphine Oxides

ALI NAGHIPOUR* and S. ABBASI
Department of Chemistry, Faculty of Science, University of Ilam, Ilam 69315, Iran
E-mail: naghipour51@yahoo.com

Synthesis and characterization of some novel N,N-dimethyl-N',N''-diaryl-phosphoramides, $Me_2NP(O)(NHAr)_2$ (where Ar = phenyl, 2-methylphenyl, 3-methyl-phenyl and 4-methylphenyl, compounds **1-4**, respectively), may act as insecticides or have other useful biological activities are reported. These compounds were prepared by the reaction of N,N-dimethylphosphoramido dichloride and the appropriate amines. They strength of aromatic amines and the effects of aromatic amines on the P-NMe_2 bond are explained and a reasonable correlation between ^{31}P chemical shifts and (P=O) vibration frequencies is identified.

Key Words: Phosphoramide, Synthesis, NMR, IR.

INTRODUCTION

Although the early history of phosphoramides goes back to 1903, they are still an interesting research area in chemistry due to their importance in biological science (with respect to the importance of nucleic acids, coenzymes in living systems) and in industry as plasticizers, flame retardants, reagents for the preparation of organophosphorus polymers in solvent extraction of heavy metals and as separation agents for enantiomers[1-3]. A large number of organophosphorus compounds are known to act as insecticides. For example, the activity of O,O-diethyl-O-(*p*-nitrophenyl)thionophosphate (E605, Parathion) as an insecticide was recognized in 1945. The catalytic activity of organophosphorus acid amides in reactions leading to thiosemicarbazides was also known[4,5].

The preparation and applications of phosphoramides have been investigated by many researchers[6,7]. The compound N,N-diphenylphosphoramido chloride is used in the synthesis of donor molecules, which may be used together with template and immobilized acceptor molecules for enzymatic extension (T4 DNA ligase) of immobilized DNA fragments[7]. Herein, the synthesis and characterization of N,N-dimethyl-N',N''-diphenylphosphoramide (**1**), N,N-dimethyl-N',N''-di-*o*-tolylphosphoramide (**2**), N,N-dimethyl-N',N''-di-*m*-tolylphosphoramide (**3**) and N,N-dimethyl-N',N''-di-*p*-

tolylphosphoramide (**4**) (Fig. 1) and the $^{3}J_{PNCH}$ coupling constants and ^{31}P chemical shifts $\delta(^{31}P)$ of these compounds have also been reported.

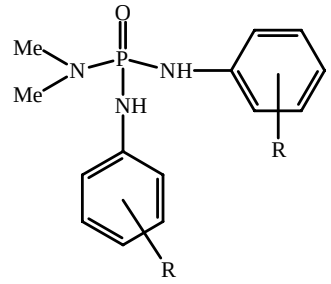

Fig. 1. Structure for N,N-dimethyl-N',N''- diarylphosphoramides; R = H (**1**), *o*-Me (**2**), *m*-Me (**3**), *p*-Me (**4**)

EXPERIMENTAL

Organophosphorus compounds are potentially neurotoxic and they should only be handled with proper safety precautions. ^{31}P NMR spectra were recorded on Jeol JNM-EX90A FT-NMR and Bruker Dry Avance 500 FT-NMR instruments, respectively; chemical shifts are reported in ppm (^{31}P relative to external 85 % H_3PO_4). All NMR spectra were obtained at 27°C. Chemicals were obtained from Merck. Aniline, *o*-toluidine and *m*-toluidine were distilled before use. Other materials were used without further purification. N,N-dimethylphosphoramido dichloride was prepared as described in the literature[8].

N,N-dimethyl-N',N''-diphenylphosphoramide (1): Aniline (4.0 mmol) dissolved in benzene (3.5 mL) was added dropwise with stirring to a solution of N,N-dimethylphosphoramido dichloride (1.0 mmol) in benzene (3.5 mL) at room temperature. The reaction mixture was stirred for 1 h, then allowed to stand for 48 h at room temperature to ensure complete reaction. Aniline hydrochloride was then removed by filtration and washed with benzene (2 × 2.0 mL). The filtrate and washings were distilled under vacuum and after removal of the benzene, the remaining solid was washed successively with carbon tetrachloride, dilute hydrochloric acid and finally with water until the washings gave a negative chloride test. The solid was dissolved in a minimum volume of ethanol or isopropyl alcohol to give crystals of **1**, which were purified by recrystallization from ethanol-carbon tetrachloride (1:1) to give colourless needles. Yield: 1.54 g (56 %), m.p. 184-186ºC; Anal. Caclcd. for $C_{14}H_{18}N_3OP$: C, 61.08; H, 6.59; N, 15.26; Found: C, 60.50; H, 6.52; N, 15.17; IR (KBr, cm^{-1}): 3276 (s), 3007 (w), 2996 (w), 1595 (s), 1481 (s), 1400 (s), 1284 (s), 1228 (s), 1160 (s), 1076

(m), 999 (s), 914 (s), 829 (m), 750 (s), 694 (s), 623 (s), 595 (m), 489 (m), 449 (s); NMR: ^{31}P ($CDCl_3$) δ + 8.25 (s); ^{1}H ($CDCl_3$) δ 2.75 (d, J = 9.85 Hz, 6H, $(CH_3)_2N$), 5.60 (2H, NH), 7.07 (10H, Ar).

N,N-dimethyl-N',N''-di-*o*-tolylphosphoramide (2): This compound was obtained by reaction of N,N-dimethylphosphoramido dichloride (1.0 mmol) and *o*-toluidine (40 mmol) as described above for **1**, but here the only recrystallization agent used was ethanol. Yield: 1.27 g (42 %), m.p. 171-173ºC; Anal. Calcd for $C_{16}H_{23}N_3OP$: C, 63.35; H, 7.31; N, 13.85; Found: C, 63.22; H, 7.40; N, 13.80; IR (KBr, cm^{-1}): 3456 (s), 3234 (s), 2972 (w), 2878 (w), 1585 (s), 1500 (s), 1404 (s), 1280 (s), 1240 (s), 1162 (s), 1053 (w), 997 (s), 918 (s), 838 (w), 811 (w), 746 (s), 690 (m), 621 (m), 549 (m), 464 (m), 433 (w); NMR: ^{31}P ($CDCl_3$) δ + 8.93 (s); ^{1}H ($CDCl_3$) δ 2.18 (s, 6H, CH_3Ar), 2.77 (d, J = 10.33 Hz, 6H, $(CH_3)_2N$), 5.38 (d, J = 9.9 Hz, 2H, NH), 7.20 (m, 8H, Ar).

N,N-dimethyl-N',N''-di-*m*-tolylphosphoramide (3): Similarly, treatment of *m*-toluidine (4.0 mmol) with N,N-dimethylphosphoramido dichloride (1.0 mmol) in benzene (7.0 mL) gave a white powder and a solution of **3**. For removal of *m*-toluidine hydrochloride, distilled water (10.0 mL) was added to the mixture and then the aqueous and organic layers were separated from each other. After drying the organic layer using $MgSO_4$ the remaining solvent was removed from the solution under vacuum. The solid was recrystallized from ether-*n*-decane to give the title compound **3** as a white powder, yield 2.06 g (68 %), m.p. 117-119ºC; Anal. Calcd. for $C_{16}H_{23}N_3OP$: C, 63.35; H, 7.31; N, 13.85; Found: C, 63.25; H, 7.38; N, 13.90; IR (KBr, cm^{-1}): 3361 (s), 3147 (s), 2986 (w), 2955 (w), 1608 (s), 1479 (s), 1367 (s), 1294 (s), 1200 (s), 1168 (s), 1093 (w), 1070 (w), 1001 (s), 958 (s), 858 (w), 711 (s), 988 (m), 619 (m), 567 (w), 505 (s), 470 (w); NMR: ^{31}P ($CDCl_3$) δ + 7.62; ^{1}H ($CDCl_3$) δ 2.19 (s, 6H, CH_3Ar), 2.73 (d, J = 9.89 Hz, 6H, $(CH_3)_2N$), 5.86 (d, J = 9.9 Hz, 2H, NH), 6.95 (m, 8H, Ar).

N,N-dimethyl-N',N''-di-*p*-tolylphosphoramide (4): This compound was obtained by reaction of N,N-dimethylphosphoramido dichloride (1.0 mmol) and *p*-toluidine (4.0 mmol) as described above for **3**. The product was purified by recrystallization from ethanol, yield 1.27 g (72 %), m.p. 171-173ºC; Anal. Calcd. for $C_{16}H_{23}N_3OP$: C, 63.35; H, .31; N, 13.85; Found: C, 63.30; H, 7.38; N, 13.93; IR (KBr, cm^{-1}): 3273 (s), 2912 (s), 1876 (w), 1614 (s), 1514 (s), 1450 (s), 1381 (s), 1308 (m), 1275 (s), 1228 (s), 1171 (s), 1072 (m), 1001 (s), 920 (s), 845 (w), 810 (s), 765 (w), 692 (m), 636 (s), 590 (s), 509 (m), 447 (s); NMR: ^{31}P ($CDCl_3$) δ + 8.23; ^{1}H ($CDCl_3$) δ 2.30 (s, 6H, CH_3Ar), 2.70 (d, J = 10.11 Hz, 6H, $(CH_3)_2N$), 5.86 (d, J = 11.7 Hz, 2H, NH), 6.97 (m, 8H, Ar).

RESULTS AND DISCUSSION

The preparation of organophosphorus compounds containing (P–N) bonds has been extensively investigated previously[1-6,8-16]. In this work, standard methods for the preparation of phosphoryl triamides were investigated[10,11]. Organophosphorus compounds containing two different (P–N) bonds were prepared in two stages. The first step was the preparation of an N-substituted phosphoramidic dichloride, $Me_2NP(O)Cl_2$, which has been generally synthesized by treatment of an amine or an amine hydrochloride with phosphorus oxychloride[5-8,10,11]. The reactivity of chlorine atoms towards nucleophilic substitution was decreased in phosphorus amides as compared with phosphoryl chloride. The reactivity of N-substituted phosphoramidic dichlorides will be largely governed by the electronic effects[6] of the basicity of the original amine, *e.g.* $(CH_3)_2NH$. In the second stage, N,N-dimethyl-N',N''-diarylphosphoramides, $Me_2NP(O)(NHAr)_2$ were synthesized by reaction of the corresponding aromatic amines with N,N-dimethylphosphoramido dichloride.

$$POCl_3 + Me_2NH\cdot HCl \rightarrow Me_2NP(O)Cl_2 + 2HCl \quad (1)$$

$$Me_2NP(O)Cl_2 + 4ArNH_2 \rightarrow Me_2NP(O)(NHAr)_2 + 2ArNH_2.HCl \quad (2)$$

In the second stage, the rate of reaction is slow because of reduction in reactivity of $Me_2NP(O)Cl_2$ relative to $POCl_3$ and to ensure complete reaction. The reactions were allowed to proceed for further 48 h. In recent years much attention has been devoted to spectroscopic studies of organophosphorus compounds[1,13-18]. Long range ^{31}P-^{1}H spin-spin couplings in benzyl and tolyl phosphorus compounds were reported previously. Griffin and Gorden[16] have interpreted the long-range couplings, in tolyl- and phosphonium salts, phosphates and phosphine oxides on the basis of an overlap hyperconjugation coupling mechanism. An alternative model for the coupling behaviour in these systems is suggested by their geometry. Examination of Fisher-Hirshfeder-Taylor models of the benzylphosphorus compounds indicates that the phosphorus atom lies over the inner circumference of the aromatic ring and thus, over the π-orbital[17]. Examination of compounds of the general formula $Me_2NP(O)(NHAr)_2$ failed to show any evidence for long range coupling. Thus, the phosphorus resonance of the *o*-, *m*- and *p*-tolyl derivatives **2**, **3** and **4** doesn't show coupling with methyl on the aryl groups and only is a septet due to hydrogens of dimethylamine group. Here the proposed range coupling mechanism is not completely satisfactory because the long range coupling depends on the nature of phosphorus atom and geometry of the compounds.

On the other hand, substitution of aromatic amines for the chlorine in $Me_2NP(O)Cl_2$ decreases the d_π-p_π contribution in P-NMe_2 ((ArNH=P(O)), compared to P-NHAr (ArNH=P(O)). This is confirmed, first by a decrease

in the coupling constant of phosphorus with the aliphatic hydrogens in NMe_2 ($^3J_{PNCH}$), second, by a shift of the phosphorus chemical shift to higher field and fourth. The general trends in the magnitude of J_{PNCH} of the prepared compounds (Table-1) are in agreement with this suggestion[19-22]. This qualitative argument is extended to ^{31}P chemical shifts and as shown in Table-2, these data support the changes in substituents to phosphorus bonding.

TABLE-1
J_{PNCH} VALUES OF PREPARED COMPOUNDS

Compound	J_{PNCH}, (Hz)
$Me_2NP(O)Cl_2$	15.70
(*o*-$MeC_6H_4NH)_2P(O)NMe_2$	10.33
$(C_6H_5NH)_2P(O)NMe_2$	9.98
(*m*-$MeC_6H_4NH)_2P(O)NMe_2$	9.89
(*p*-$MeC_6H_4NH)_2P(O)NMe_2$	10.11

TABLE-2
^{31}P CHEMICAL SHIFTS OF PREPARED COMPOUNDS

Compound	$\delta^{31}P$ (ppm)
(*m*-$MeC_6H_4NH)_2P(O)NMe_2$	7.62
(*p*-$MeC_6H_4NH)_2P(O)NMe_2$	8.23
$(C_6H_5NH)_2P(O)NMe_2$	8.25
(*o*-$MeC_6H_4NH_2)P(O)NMe_2$	8.93
$Me_2NP(O)Cl_2$	20.54

On the other hand, in the series, $Me_2NP(O)Cl_2$ ($\delta^{31}P$ = 20.54 ppm), (*o*-$MeC_6H_4NH_2)_2P(O)NMe_2$ ($\delta^{31}P$ = 8.93 ppm), $(C_6H_5NH_2)_2P(O)NMe_2$ ($\delta^{31}P$ = 8.25 ppm), (*m*-$MeC_6H_4NH_2)_2P(O)NMe_2$ ($\delta^{31}P$ = 8.23 ppm), there is an obvious decrease in phosphorus chemical shifts as the nucleophilic strength of the aromatic amines increases, in agreement with results previously reported by Wagner who found that PO bond characters are consistent with the electronegativity of the Y group in symmetrically substituted phosphoryl compounds, POY_3[23].

Conclusions

N,N-dimethyl phosphoramido dichloride [$Me_2NP(O)Cl_2$] as an initial reagent was obtained by the reaction of phosphoryl chloride and dimethyl amin hydrochloride. Phosphortriamides of N,N-dimethylphosphoramido dichloride $Me_2NP(O)(NHAr)_2$ (Ar = phenyl, 2-methyl phenyl, 3-methyl phenyl and 4-methyl phenyl were characterized by solution study obtained

from the reaction of corresponding amines and N,N-dimethylphosphoramido dichloride. In this study, we have changed chlorine with aromatic amines and observed the reducing in coupling of phosphorus-hydrogen and the upfield chemical shift in ^{31}P resonance.

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