FORMYLPHOSPHORAMIDATES¹

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Abstract—Formylphosphoramidates are new members of a rare class of phosphorus compounds. Isolation and characterization of these materials by instrumental and chemical means is discussed. Proof of structure for dibutyl formylphosphoramidate was achieved by reduction to dibutyl N-methylphosphoramidate.

IT was reported in the preceding paper³ that certain phosphorus azides (I) react with straight chain vinyl ethers (II) to give, after loss of diazomethane, N-phosphorylated imidates (III).

 $\begin{array}{cccc} R_{3}P(O)N_{3}+CH_{3}\hline CHOR'\rightarrow R_{5}P(O)N\hline CHOR'+CH_{3}N_{3}\\ I & II & III \\ (a) R=C_{3}H_{5}O & (d) R=C_{3}H_{5}O, R'=(CH_{3})_{5}CH\\ (b) R=C_{4}H_{5}O & (e) R=C_{3}H_{5}O, R'=(CH_{3})_{5}CHCH_{3}\\ (c) R=C_{6}H_{5} & (f) R=C_{4}H_{5}O, R'=(CH_{3})_{5}CHCH_{3}\\ (g) R=C_{6}H_{5}, R'=(CH_{3})_{5}CH \\ \end{array}$

The latter compounds (IIId, -e, -f and -g) readily incurred hydrolytic cleavage upon exposure to the atmosphere, or on treatment with hot water and yielded the formylphosphoramidates (IV) and alcohols (R'OH). Thus, diethyl (IVa), dibutyl formyl phosphoramidate (IVb) and diphenyl formylphosphinic amide (IVc) were obtained, respectively. The alcohols $[R' = (CH_3)_2CH, (CH_3)_2CHCH_2]$ were identified by IR and GLC analyses. Compounds IVa, -b and -c were characterized by elemental

 $R_{s}P(O)N \Longrightarrow CHOR' + H_{s}O \rightarrow R_{s}P(O)NHCH \Longrightarrow O + R'OH$ III IV
(a) $R = C_{s}H_{s}O$ (b) $R = C_{4}H_{5}O$ (c) $R = C_{6}H_{5}$

(Table 1) and spectral analyses and by chemical transformations. The IR spectra (Table 2) showed strong bands at 3448–2941 (broad, NH), 1709 (C=O), and 1250 cm⁻¹ (P \rightarrow O). The IR spectra of solutions of one compound (IVa) in carbon tetrachloride indicated that the intensity of the broad band at 3448–2941 cm⁻¹ decreased with increasing dilution and a sharp doublet appeared at 3448 and 3356 cm⁻¹ (free NH). The carbonyl (1709 cm⁻¹) and the phosphoryl (1250 cm⁻¹) bands also displayed some

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⁸ K. D. Berlin and M. A. R. Khayat, Tetrahedron 22, 975 (1966).

	Yield	B.p./mm	110	Found (Caic)				
Compound	%	(m.p.)	(Ĉ°)	C	н	N	P	Formula
(C ₂ H ₅ O) ₂ P(O)NHCHO IVa	50	134°/0-25	1·4368 (24)	33·0 (33·2)	6·5 (6·6)	7·4 (7·7)	17·1 (17·1)	C ₆ H ₁₃ NO ₄ P
(C4H,O)3P(O)NHCHO	58	168·5-170°/2	1·4430 (24)	46·1 (45·5)	8.6 (8.45)	6·15 (5·9)	13·0 (13·1)	C ₉ H ₂₀ NO ₄ P
(C ₆ H ₅) ₂ P(O)NHCHO IVc	47	178-180°	. ,	63·3 (63·5)	4·9 (4·9)	5.5 (5.7)	12·8 (12·7)	C ₁₈ H ₁₈ NO ₈ P

TABLE 1. SOME PHYSICAL PROPERTIES OF THE FORMYLPHOSPHORAMIDATES

		Assignments (cm ⁻¹)			
Compound	NH	C=0	P → O	Miscellaneous Bands	
IVa	3448	1709	1266, 1212	1026	
IVb	3448	1709	1266	1064, 990	
IVc	3125	1709	1220, 1190	1439 (P-C _s H _s)	

changes in shape and location. This suggests the presence of extensive intermolecular hydrogen-bonding involving the NH, the C=O, and the $P \rightarrow O$ groups possibly as



represented by V or VI. This is analogous to reported cases of hydrogen bonding in a few substituted phosphoramidates.^{4.5} It is also supported by the observation that the first two amidates IVa and IVb have b.ps and refractive indices higher than those of their corresponding parent compounds IIId and IIIf, respectively. The third amidate (IVc) was a solid. Although dialkyl N-arylphosphoramidates are known,⁴ the formyl derivatives have not been reported previously.

The NMR spectra of the amidates (IVa and IVb) were measured in carbon tetrachloride (containing TMS as internal reference). The spectrum of IVc was examined in tetramethylurea, dimethyl sulfoxide, and in a solution of NaOD in D_2O . The data are included in Table 3.

⁴ M. I. Kabachnik, V. A. Gilyarov, C. Cheng-tieh, and E. I. Matrosov, *Izvest. Akad. Nauk S.S.S.R.*, Otdel. Khim. Nauk 1504 (1962). Recent reviews are available on organophosphorus chemistry and data is included on the brief knowledge of this area. Methoden der organischen Chemie (Edited by E. Muller) Vol. 12; parts 1 and 2; K. Sasse, Organische Phosphorverbindungen. Georg Thieme Verlag, Stuttgart (1962 and 1965).

^{*} L. J. Beliamy and L. Beecher, J. Chem. Soc. 1701 (1952).

		Chemical Shift Parameters (δ, ppm; J, c/s)						
Compound	NH	CH=O	C ₆ H ₆	CH3O	CH,CH,	CH,		
IVa*	8·63 (b)	8·36 (d, J = 7)		4.08 (s, J = 7.5)		1·34 (t, J = 7)		
IVa•	none	8·51 (d, J = 12)		4·18 (q, J = 8)				
IVb•	9·29 (b)	8·50 (d, J = 6·5)		4·15 (q, J = 7)	1∙60 (m)	0.95 (t, J = 6.5)		
IVc ^d	10·20 (b)	8·50 (d, J = 9)	7·33 7·66 (m)					
IVc•	10-65 (b)	8·73 (m)	8·10 7·73 (m)					
IVơ	none	8·45 (d, J = 13)	7·04 7·40					

TABLE 3. NMR DATA FOR THE SUBSTITUTED FORMYLPHOSPHORAMIDATES

• In CCl₄ with tetramethylsilane (TMS) as an internal standard: b, broad; d, doublet; t, triplet; q, quintet; m, multiplet; s, sextet.

^b In a solution of NaOD in D₁O with TMS as an external reference.

• In tetramethylurea with TMS as an external reference.

⁴ In dimethyl sulfoxide with TMS as an external reference.

The positions of the broad signals at $\delta 8.63$, 9.29, and 10.65 (NH), and those of the doublets at $\delta 8.36$, 8.50 and 8.73 (--CH=O), in the spectra of IVa, and -b, and c respectively, are consistent in molecules with a system such as $\geq P$ --NH--CH=O.⁶ The proton attached to the carbonyl groups in N,N-dimethylformamide exhibits a low-field signal at $\delta 8.02$ (in CCl₄).⁷ Further, upon recording the spectra of IVa and IVc in a solution of NaOD in D₂O, distinct and sharp doublets (J = 12-13 c/s) were shown at $\delta 8.51$ and 8.45 (relative to $\delta_{DOH} 4.88$), respectively. These signals were attributed to the proton on the carbonyl carbon atom in the salt VII and the splitting is probably by phosphorus. The location and splitting patterns of other signals in the

H

$$B = 0$$

 $R_{3}P(0)NHCHO + NaOD \rightarrow R_{3}P(0)N-C=0$, $Na + DOH$
 IV VII
(a) $R = C_{3}H_{4}O$, (b) $R = C_{4}H_{4}O$, (c) $R = C_{4}H_{4}$

spectra of the amidates correspond to the rest of the protons in the respective compounds (IVa, -b, and -c).

The UV data of the amidates (IVb and -c) are included in Table 4. The amidate IVb showed an absorption band at 221.3 m μ which upon addition of alkali underwent a bathochromic shift to 224.3 m μ . Similarly, the amidate IVc had two strong bands of equal intensities at 212.5 m μ and 222.5 m μ ; after addition of alkali a single strong

- The NMR spectra of CH₃NHCHO (in CCl₄) shows a signal at δ 8·11 which may be a superimposition of the proton signals in NH and CHO [V. J. Kowalewski and D. G. Kowalewski, J. Chem. Phys. 33, 1794 (1960)]. Further, the coupling effect of phosphorus is reported to be transmitted to a remotely situated proton as in ⇒P-N-C-H [G. Singh and H. Zimmer, J. Org. Chem. 29, 1579 (1964); *Ibid.* 30, 417 (1965)].
- ⁷ N. S. Bhacca, L. F. Johnson and N. N. Shoolery, *NMR Spectra Catalog* Vol. 1; spectrum No. 39. Varian Associates, Palo Alto, California.

Compound	λ_{max} (m μ)	Log e	Solvent
IVb	221.3 (shoulder)	2.057	Ethanol
	224.4	2.531	Ethanol and KOH
IVc	212.5	4.288	Ethanol
	222.5	4.288	
	253-3	2.931	
	259-7	3.125	
	265.8	3.243	
	272.8	3.167	
	227.5	4·247	Ethanol ^a and
			кон

TABLE 4. UV SPECTRAL DATA OF THE FORMYLPHOSPHORAMIDATES IVb AND IVC

" The same benzenoid bands were also observed.

band appeared at 227.5 m μ . This phenomenon, probably, was a result of the extended conjugation in the salt VIII of the amidates.

$$R_{s}P(O)NHCHO \xrightarrow{KOH} R_{s}P \xrightarrow{O} O \\ -H_{s}O \xrightarrow{O} O \\ CH, K^{\oplus} \\ N \\ VIII \\ (a) R = C_{s}H_{s}O \quad (b) R = C_{s}H_{s}O \quad (c) R = C_{s}H_{s}$$

The UV spectra of the phosphorylacetylmethane (IXa) and the diphosphorylmethane (IXb) and those of their ions Xa and Xb, respectively, have been studied in THF solution by Cotton *et al.*⁸ and are compared with the UV spectra of acetylacetone IXc and its ion Xc.⁹



It was found that the ions X absorb at longer wavelengths than do their parent compounds (IX), a phenomenon which is attributed to the extended π -orbital systems which undergo π - π * transitions. Although the UV spectra of IV and VIII were run in a different solvent (namely EtOH, which is preferred to THF since the latter rapidly

* F. A. Cotton and R. A. Schunn, J. Amer. Chem. Soc. 85, 2394 (1963).

^a R. H. Holm and F. A. Cotton, J. Amer. Chem. Soc. 80, 5658 (1958).

absorbs moisture), the observed bathochromic shift in the absorption of VIII is consistent with expectation and with the reported⁸ observation.

As was pointed out previously, the formylamidates (IV) have an acidic hydrogen, and thus can form salts (such as VII and VIII) and react with metallic sodium with the evolution of hydrogen. The compounds are similar to other dialkyl N-acylphosphoramidates.¹⁰ For example, a derivative such as $(C_2H_5O)_2P(O)NHCOCH_3$ has been found to possess acidity [pKa = 9.46] comparable to that of phenol.⁴

In an effort to determine whether compounds IV exist in the imide form (XI) the IR, UV and NMR spectra were examined. The absence of a strong band in the region 1325-1385 cm⁻¹ (P=N)^{4.11} of the IR and the absence of any absorption in the region 230-340 m μ (in the UV spectrum of IVb) suggest that the compounds were predominantly in the amide form (IV). This is corroborated by the observation in the NMR spectrum of IVa or IVc, that removal of the proton (by addition of alkali to IVa or



IVc; see structure VII) affects the coupling constant of the doublet for the proton in the aldehyde group suggesting that the acidic proton is situated on the adjacent nitrogen and not bonded to the phosphoryl oxygen as in XI.¹² The acidities of some N-acylphosphoramidates have been measured as cited previously, and are found to be much lower than those of phosphorus oxy acids (pKa = about 2-4).⁴ By analogy, the formylphosphoramidates (IV) might be expected to have nearly the same acidity as that of ($C_{2}H_{5}O$)₂P(O)NHCOCH₃ and therefore do not exist in the imidol form (XI). The presence of a tautomer such as XII may be excluded on the grounds of the evidence



presented and the fact that the IR band at 1709 cm⁻¹ in IV (Table 2) is better ascribed to a carbonyl rather than a C=N group since the latter group absorbs at a much lower frequency.¹¹

Studies on XIII have shown that it can exist in the other tautomeric form (XIV).13

- ¹⁰ M. I. Kabachnik, V. A. Gilyarov and E. M. Popov, Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk 945 (1961).
- ¹¹ L. J. Bellamy, The Infrared Spectra of Complex Molecules. J. Wiley, New York (1958).
- ¹³ Although the chemical shift is highly solvent dependent, P-O-H couplings (as in XI) are usually broad singlets at low field; see J. R. Ferraro and P. F. Peppard, J. Phys. Chem. 67, 2639 (1963); K. D. Berlin and M. Nagabhushanam, Proc. Okla. Acad. Sci. 46, In Press (1965).
- ¹⁸ L. Larson and L. -E. Tammelin, Acta Chem. Scand. 15, 349 (1961).



In this case the presence of a phenyl group, and probably intramolecular hydrogenbonding, are expected to have an appreciable influence on the equilibrium in favour of XIV.

Attempted synthesis of IV. Efforts to synthesize compounds IV were unsuccessful via the reaction of the corresponding chloride (XV) and formamide in the presence of

 $R_{s}P(O)Cl + H_{s}NCHO \xrightarrow{-HCl} IV \xrightarrow{}$ $XV \qquad R_{s}P(O)Cl \qquad \downarrow$ $XV + R_{s}P(O)NHCHO \xrightarrow{} CO + R_{s}P \rightarrow O + other products$ IV(a) $R = C_{s}H_{s}O$ (b) $R = C_{4}H_{s}O$ (c) $R = C_{6}H_{5}$

triethylamine. It was recognized that the intermediate (IV) would have an acidic hydrogen and subsequent attack by a second molecule of the phosphorus chloride (XV) could ensue rapidly. In one example (XVb), a complex mixture formed. Tributyl phosphate and carbon monoxide were identifiable components. Similar results were obtained when XVb and pure IVb were allowed to condense in the presence of triethylamine. Likewise XVa gave triethyl phosphate, carbon monoxide and a mixture of many components. A complex mixture of at least five components (analyzed by TLC) was also obtained from treatment of XVc with formamide in the presence of triethylamine. One identifiable product, which precipitated out of the reaction mixture, was the anhydride of diphenylphosphinic acid. Survival of the latter compound in the mixture probably was assisted by its low solubility. Although all reagents were freshly distilled, the reactants are hygroscopic and partial hydrolysis of XVc may have occurred to give the anhydride.

Treatment of IVb (obtained from IIIf) with dilute acid produced 1-butanol, formic acid and phosphoric acid. Ammonia was detected in the mixture after the

$$(C_4H_9O)_8P(O)NHCHO \xrightarrow{acid} \xrightarrow{base} 2C_4H_9OH + NH_8 + PO_4 \equiv + HCO_8H$$

IVb

latter was made alkaline. In connection with the above hydrolysis, it was observed that initial treatment of IVb with base did not afford ammonia, probably as a result of the formation of a stable anion intermediate such as XVI or XVII. Acidification of the

$$IVb \xrightarrow{OH} 2C_4H_4OH + \begin{bmatrix} O & O \\ P \\ O & N-CHO \end{bmatrix} \xrightarrow{=} PO_4 \xrightarrow{=} + [NH-CHO]^{-1}$$

XVI XVII

992

mixture (or initial treatment of IVb with acid) followed by warming, and subsequent treatment with alkali yielded ammonia. Further confirmation of the structure of IVb was achieved by reduction of the latter compound with LAH to the known dibutyl N-methylphosphoramidate (XVIII).¹⁴ It is noteworthy that the latter reduction did not take place with NaBH₄. This is probably due to the fact that NaBH₄ is a less

$$\frac{LAH}{(C_4H_9O)_3P(O)NHCH_3}$$
XVIII

reactive reagent than LAH. The latter reagent reduces some carboxylic acids to primary alcohols whereas the former does not.¹⁵

EXPERIMENTAL

All b.ps and m.ps are uncorrected. The microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee. The IR, UV and NMR spectra were determined on a Beckman IR-5, a Cary 14, and a Varian Model A-60 spectrometer, respectively.

The amidates (IVa and b) were prepared (as described previously³) from the phosphorylated imidates (IIId and f) by hydrolysis with hot water and were purified by distillation. The alcohols, the volatile products of hydrolysis, were identified by IR and GLC (Hy Fi hydrogen flame unit produced by Wilkens Instrument, Inc., Walnut Creek, California). The third amidate IVc was prepared as described below.

Diphenyl formylphosphinic amide (IVc). A solution of IIIg (1.3 g, 0.0045 mole) in ether (50 ml) was left exposed to the atmosphere overnight; a white solid was deposited (0.5 g, 47% yield). It was crystallized from CHCl₈, m.p. 178–180°, and was characterized as IVc by elemental and spectral analyses (Tables 1, 2, 3 and 4).

Hydrolysis of IVb. The IVb (2 g; 0.0084 mole) was heated with 2N HCl on a steam bath for 2 hr. The volatile matter was then distilled; GLC analysis of the latter mixture indicated the presence of butanol. Formic acid was detected by conventional chemical tests.¹⁵ The phosphate ion was also detected in the aqueous layer.¹⁷ The aqueous mother liquor was made basic and warmed and ammonia was evolved. The latter compound was not evolved when IVb was initially treated with hot dilute alkali.

Reduction of IVb with LAH. A solution of IVb (1.0 g, 0.004 mole) in dry ether (10 ml) was added to a stirred suspension of LAH (0.5 g) in dry ether (20 ml). After the addition was complete, the reaction mixture was boiled for an additional 2 hr, cooled, and cautiously decomposed with ice/-dil. HCl. The organic layer was separated, combined with the ethereal extracts of the aqueous layer and dried (MgSO₄). Removal of the solvent left an oil (0.65 g; 70% yield) which was identified by IR and NMR spectroscopy as XVIII, b.p. 130-132°/0.25 mm, reported¹⁴ b.p. 116-119°/0.5 mm. An authentic specimen of the latter compound (which is not commercially available) was synthesized from dibutyl phosphorochloridate and methylamine.¹⁴ Treatment of IVb with NaBH₄ in EtOH resulted in the recovery of unreacted starting material.

Attempted synthesis of IVb. A solution of XVb (11.5 g, 0.05 mole) in monoglyme (30 ml) was added dropwise into a stirred and cooled (0.5°) solution of formamide (1.13 g; 0.025 mole) and triethylamine (7 ml; 0.06 mole) in monoglyme (100 ml). The amine hydrochloride precipitated slowly. The reaction mixture was kept at room temp for several hrs; meanwhile the exit gases were allowed to pass through a suspension (brown) of PdCl_a in water. The gradual formation of black Pd was considered as a positive test for the slow evolution of CO.¹⁸ The mixture was filtered, the

- ¹⁶ Boron, Metallo-Boron Compounds, and Boranes (Edited by R. M. Adams) p. 425. Interscience, New York (1964).
- ¹⁶ F. Feigl, Spot Tests in Organic Analysis (5th English Edition) p. 340. Elsevier, New York (1956).
- ¹⁷ J. Nordmann, Qualitative Testing and Inorganic Chemistry p. 392. J. Wiley, New York (1957).

¹⁸ W. Ruske and M. Keilert, Chem. Ber. 94, 2695 (1961).

¹⁴ A. C. Poshkus and J. E. Herweh, J. Amer. Chem. Soc. 79, 6127 (1957).

solvent was removed, and the residual oil was distilled (at 1.0 mm press) giving the following fractions: (a) 56-104° (0.6 g); (b) 104-106° (0.8 g); (c) 106-114° (1.7 g); and (d) 114-126° (3 g), and a large amount of tarry residue (water soluble). IR analysis indicated that fraction (a) contained mainly unreacted formamide and that all fractions contained varying amounts of unknown materials. Fraction (d) was redistilled and gave an oil (b.p. 114-114.5°/1.2 mm, n_D^{ss} 1.4220) which was identified (IR) as tributyl phosphate (reported¹⁸ b.p. 150°/10 mm, n_D^{ss} 1.4224).

Similarly, a solution of diphenylphosphinic chloride (4 g) in ether was allowed to react with a solution of formamide (0.76 g) and triethylamine (1.75 g) in ether. A white solid was immediately formed. After 2 hr the solid was filtered, washed with water [to remove $(C_1H_s)_8N$ ·HCl] several times, and crystallized from CCl₄. The solid (4.5 g) was identified (IR) as $[(C_6H_s)_8P(O)]_9O$, m.p. 140–143°, reported¹⁰ m.p. 143°. Analysis of the mother liquor by TLC (silica gel with acetone-chloroform) indicated the presence of at least five components.

¹⁹ D. P. Evans, W. C. Davies, and W. J. Jones, J. Chem. Soc. 1310 (1930).

²⁰ K. Moedritzer, J. Amer. Chem. Soc. 83, 4381 (1961).